Application Search

Fredman 09/829,467

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ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                         2001:753071 HCAPLUS
DOCUMENT NUMBER:
                         135:303873
                         Entered STN: 16 Oct 2001
ENTRY DATE:
TITLE:
                         Fluorescent labeled nucleotides, synthesis and
                         application as probes and primers
INVENTOR(S):
                         Shinoki, Hiroshi; Inomata, Hiroko; Kojima, Masayoshi;
                         Sudo, Yukio; Seshimoto, Osamu
PATENT ASSIGNEE(S):
                         Fuji Photo Film Co., Ltd., Japan
                         Jpn. Kokai Tokkyo Koho, 14 pp.
SOURCE:
                         CODEN: JKXXAF
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         Japanese
INT. PATENT CLASSIF.:
            MAIN:
                         C07H019-10
       SECONDARY:
                        C07H019-20; C07H021-00; C09K011-06; C12N015-09;
                        C12Q001-68; G01N033-58; C07D209-08; C07D209-30;
                        C07D403-06; C07D403-14
CLASSIFICATION:
                        28-1 (Heterocyclic Compounds (More Than One Hetero
                        Atom))
                        Section cross-reference(s): 3, 9
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
                                                                  DATE
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                               _____
                                           ______
     JP 2001288197
                         A2
                               20011016
                                          JP 2000-107675
                                                                  20000410
                                          US 2001-829467
     US 2002064782
                         A1
                               20020530
                                                                  20010409 <--
     EP 1152008
                         A2
                                          EP 2001-107864
                               20011107
                                                                  20010410
     EP 1152008
                         А3
                               20020320
     EP 1152008
                        В1
                               20050209
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.:
                                           JP 2000-107675
PATENT CLASSIFICATION CODES:
 PATENT NO.
            CLASS PATENT FAMILY CLASSIFICATION CODES
                       JP 2001288197
                ICM
                       C07H019-10
                       C07H019-20; C07H021-00; C09K011-06; C12N015-09;
                ICS
                       C12Q001-68; G01N033-58; C07D209-08; C07D209-30;
                       C07D403-06; C07D403-14
                IPCI
                       C07H0019-10 [ICM,7]; C07H0019-20 [ICS,7]; C07H0021-00
                       [ICS,7]; C09K0011-06 [ICS,7]; C12N0015-09 [ICS,7];
                       C12Q0001-68 [ICS,7]; G01N0033-58 [ICS,7]; C07D0209-08
                       [ICS,7]; C07D0209-30 [ICS,7]; C07D0403-06 [ICS,7];
                       C07D0403-14 [ICS,7]
 US 2002064782
                       C12Q0001-68 [ICM,7]; C07H0021-04 [ICS,7]; C12P0019-34
                IPCI
                       [ICS, 7]
                       C07H0021-00 [I,A]; C07H0021-00 [I,C]
                IPCR
                NCL
                       435/006.000
                ECLA
                       C07H021/00G
 EP 1152008
                IPCI
                       C07H0019-06 [ICM, 6]; C07H0019-16 [ICS, 6]; C07H0021-00
                       [ICS, 6]; C12Q0001-68 [ICS, 6]; G01N0033-53 [ICS, 6]
                IPCR
                       C07H0021-00 [I,A]; C07H0021-00 [I,C]
                ECLA
                       C07H021/00G
OTHER SOURCE(S):
                        MARPAT 135:303873
ABSTRACT:
The present invention provides a fluorescent substance which is represented by
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a formula: A-B-C wherein A is a residue of natural or synthetic nucleotide, oligonucleotide, polynucleotide, or derivative thereof, and binds to B at a base moiety in said residue; B is a divalent linking group or a single bond; and C is a derivative of fluorescent dye having 0 or 1 sulfonate or phosphate moiety. Fluorescent dye is cyanine, melocyanine, or styryl. Preferably A is AMP, ADP, ATP, GMP, GDP, GTP, CMP, CDP, CTP, UMP, UDP, UTP, TMP, TDP, TTP, 2-Me-AMP, 2-Me-ADP, 2-Me-ATP, 1-Me-GMP, 1-Me-GDP, 1-Me-GTP, 5-Me-CMP, 5-Me-CDP, 5-Me-CTP, 5-MeO-CMP, 5-MeO-CDP, 5-MeO-CTP. B is preferably -CH2-, -CH=CH-, triple bond, -CO-, -O-, -S-, -NH-, or aminoaryl. Synthesis of labeled nucleic acids using the nucleotides via reverse transcription, terminal transferase reaction, random prime method, PCR, or nick translation, is claimed. The fluorescent substance of the present invention is useful as label for nucleic acids, reagent for detecting nucleic acids, or diagnostic reagent. Kits for nucleic acid detection are claimed. Synthesis of 8 indolenine cyanine compds. and conjugation with dUTP, and use for DNA probe preparation, are described.

SUPPL. TERM:

fluorescent labeled nucleotide synthesis probe primer; cyanine melocyanine styryl nucleotide synthesis probe primer

INDEX TERM:

Diagnosis

(agents; fluorescent labeled nucleotide synthesis and

application as probes and primers)

INDEX TERM:

Phosphates, biological studies

Sulfonates

ROLE: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(dye containing; fluorescent labeled nucleotide synthesis and

application as probes and primers)

INDEX TERM:

Cyanine dyes Fluorescent dyes

Test kits

(fluorescent labeled nucleotide synthesis and application

as probes and primers)

INDEX TERM:

Nucleotides, preparation

Oligonucleotides Polynucleotides

ROLE: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(fluorescent labeled nucleotide synthesis and application

as probes and primers)

INDEX TERM:

Nucleic acid amplification (method)

(terminal transferase reaction, use in labeled nucleic acid synthesis; fluorescent labeled nucleotide synthesis

and application as probes and primers)

INDEX TERM:

PCR (polymerase chain reaction)

Reverse transcription

(use in labeled nucleic acid synthesis; fluorescent labeled nucleotide synthesis and application as probes and primers)

INDEX TERM:

23065-05-6, Styryl

ROLE: ARG (Analytical reagent use); ANST (Analytical study);

USES (Uses)

(fluorescent labeled nucleotide synthesis and application as probes and primers)

INDEX TERM:

366451-16-3P 366451-17-4P 366451-18-5P 366451-19-6P 366451-20-9P 366451-21-0P

366451-22-1P 366451-23-2P

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ROLE: ARG (Analytical reagent use); BUU (Biological use,
                    unclassified); SPN (Synthetic preparation); ANST (Analytical
                    study); BIOL (Biological study); PREP (Preparation); USES
                    (Uses)
                       (fluorescent labeled nucleotide synthesis and application
                       as probes and primers)
 INDEX TERM:
                  56-65-5, 5'-ATP, reactions 58-64-0,
                    5'-ADP, reactions 58-97-9, 5'-UMP, reactions
                    58-98-0, 5'-UDP, reactions 61-19-8,
                    5'-AMP, reactions 63-37-6, CMP 63-38-7,
                    CDP 63-39-8, 5'-UTP 65-47-4, 5'-CTP
                    85-32-5, 5'-GMP 86-01-1, 5'-GTP
                    95-50-1, 1, 2-Dichloro benzene 122-51-0,
                    Triethyl orthoformate 146-91-8, 5'-GDP
                    365-07-1, DTMP 365-08-2, TTP
                    491-97-4, TDP 628-89-7 1173-82-6
                    , DUTP 1173-82-6D, DUTP, aminoaryl
                    1927-31-7, DATP 2056-98-6, DCTP
                    2564-35-4, DGTP 3590-36-1
                    4224-70-8, 6-Bromo hexanoic acid 14315-97-0
                    20309-92-6 25981-83-3 39923-67-6
                    39923-68-7, 2-Methyl-ADP 42467-24-3,
                    2-Methyl-ATP 52940-67-7 52988-98-4
                    76528-21-7 80677-38-9 112242-04-3
                    130536-69-5 327174-86-7
                    366451-24-3
                    ROLE: RCT (Reactant); RACT (Reactant or reagent)
                       (fluorescent labeled nucleotide synthesis and application
                       as probes and primers)
INDEX TERM:
                 366451-26-5DP, bromide 366451-27-6DP,
                   bromide 366451-28-7DP, bromide
                   ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
                    (Preparation); RACT (Reactant or reagent)
                       (fluorescent labeled nucleotide synthesis and application
                       as probes and primers)
INDEX TERM:
                 75-03-6, Ethyl iodide 62306-05-2
                   ROLE: RCT (Reactant); RACT (Reactant or reagent)
                       (reactant; fluorescent labeled nucleotide synthesis and
                       application as probes and primers)
INDEX TERM:
                 366451-25-4DP, iodide
                   ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
                    (Preparation); RACT (Reactant or reagent)
                       (reactant; fluorescent labeled nucleotide synthesis and
                      application as probes and primers)
     23065-05-6, Styryl
ΙT
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (fluorescent labeled nucleotide synthesis and application as probes and
        primers)
     23065-05-6 HCAPLUS
RN
CN
     Ethenyl, 2-phenyl- (9CI) (CA INDEX NAME)
HC== CH- Ph
     366451-16-3P 366451-17-4P 366451-18-5P
IT
     366451-19-6P 366451-20-9P 366451-21-0P
     366451-22-1P 366451-23-2P
    RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN
```

(Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(fluorescent labeled nucleotide synthesis and application as probes and primers)

RN 366451-16-3 HCAPLUS

CN 3H-Indolium, 1-(5-carboxypentyl)-2-[5-(1-ethyl-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene)-1,3-pentadienyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)

RN 366451-17-4 HCAPLUS

CN 3H-Indolium, 1-(5-carboxypentyl)-5-chloro-2-[5-[5-chloro-1,3-dihydro-1-[2-(2-hydroxyethoxy)ethyl]-3,3-dimethyl-2H-indol-2-ylidene]-1,3-pentadienyl]-3,3-dimethyl-(9CI) (CA INDEX NAME)

RN 366451-18-5 HCAPLUS

CN 3H-Indolium, 5-(aminosulfonyl)-2-[3-[5-(aminosulfonyl)-1-(5-carboxypentyl)-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1-propenyl]-1-ethyl-3,3-dimethyl- (9CI) (CA INDEX NAME)

RN 366451-19-6 HCAPLUS

CN 3H-Indolium, 1-(5-carboxypentyl)-5-chloro-2-[3-[5-chloro-1,3-dihydro-1-[2-(2-hydroxyethoxy)ethyl]-3,3-dimethyl-2H-indol-2-ylidene]-1-propenyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)

RN 366451-20-9 HCAPLUS

CN 3H-Indolium, 5-(aminosulfonyl)-2-[5-[5-(aminosulfonyl)-1-[6-[[2-[1-[2-deoxy-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-erythro-pentofuranosyl]-1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl]ethenyl]amino]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1,3-pentadienyl]-1-ethyl-3,3-dimethyl-, inner salt, trisodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

PAGE 1-A

●3 Na

PAGE 1-B

RN 366451-21-0 HCAPLUS

CN 3H-Indolium, 5-chloro-2-[5-[5-chloro-1-[6-[[2-[1-[2-deoxy-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-erythro-pentofuranosyl]-1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl]ethenyl]amino]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1,3-pentadienyl]-1-[2-(2-hydroxyethoxy)ethyl]-3,3-dimethyl-, inner salt, trisodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

PAGE 1-A

•3 Na

PAGE 1-B

RN 366451-22-1 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 5-[2-[[6-[5-(aminosulfonyl)-2-[3-[5-(aminosulfonyl)-1-ethyl-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1-propenyl]-3,3-dimethyl-3H-indolio]-1-oxohexyl]amino]ethenyl]-2'-deoxy-, inner salt, trisodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

PAGE 1-A

●3 Na

PAGE 1-B

RN 366451-23-2 HCAPLUS

CN 3H-Indolium, 5-chloro-2-[3-[5-chloro-1-[6-[[2-[1-[2-deoxy-5-0-[hydroxy[[hydroxy(phosphonoxy)phosphinyl]oxy]phosphinyl]- β -D-erythropentofuranosyl]-1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl]ethenyl]amino]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1-propenyl]-1-[2-(2-hydroxyethoxy)ethyl]-3,3-dimethyl-, inner salt, trisodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

●3 Na

PAGE 1-B

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IT
      56-65-5, 5'-ATP, reactions 58-64-0, 5'-ADP, reactions
      58-97-9, 5'-UMP, reactions 58-98-0, 5'-UDP, reactions 61-19-8, 5'-AMP, reactions 63-37-6, CMP 63-38-7, CDP 63-39-8, 5'-UTP 65-47-4, 5'-CTP 85-32-5
      , 5'-GMP 86-01-1, 5'-GTP 95-50-1, 1, 2-Dichloro benzene 122-51-0, Triethyl orthoformate 146-91-8,
      5'-GDP 365-07-1, DTMP 365-08-2, TTP 491-97-4
      , TDP 628-89-7 1173-82-6, DUTP 1173-82-6D,
      DUTP, aminoaryl 1927-31-7, DATP 2056-98-6, DCTP
      2564-35-4, DGTP 3590-36-1 4224-70-8, 6-Bromo
      hexanoic acid 14315-97-0 20309-92-6 25981-83-3
      39923-67-6 39923-68-7, 2-Methyl-ADP 42467-24-3
      , 2-Methyl-ATP 52940-67-7 52988-98-4
      76528-21-7 80677-38-9 112242-04-3
      130536-69-5 327174-86-7 366451-24-3
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (fluorescent labeled nucleotide synthesis and application as probes and
         primers)
RN
      56-65-5 HCAPLUS
      Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)
CN
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RN 58-64-0 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 58-97-9 HCAPLUS

CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 58-98-0 HCAPLUS

CN Uridine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

RN 61-19-8 HCAPLUS

CN 5'-Adenylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 63-37-6 HCAPLUS

CN 5'-Cytidylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 63-38-7 HCAPLUS

CN Cytidine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 63-39-8 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

RN 65-47-4 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 85-32-5 HCAPLUS

CN 5'-Guanylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 86-01-1 HCAPLUS

CN Guanosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

RN 95-50-1 HCAPLUS

CN Benzene, 1,2-dichloro- (9CI) (CA INDEX NAME)

RN 122-51-0 HCAPLUS

CN Ethane, 1,1',1''-[methylidynetris(oxy)]tris- (9CI) (CA INDEX NAME)

RN 146-91-8 HCAPLUS

CN Guanosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 365-07-1 HCAPLUS

CN 5'-Thymidylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 365-08-2 HCAPLUS

CN Thymidine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

RN 491-97-4 HCAPLUS

CN Thymidine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 628-89-7 HCAPLUS

CN Ethanol, 2-(2-chloroethoxy)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

 $C1CH_2-CH_2-O-CH_2-CH_2-OH$

RN 1173-82-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 1173-82-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

RN 1927-31-7 HCAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 2056-98-6 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 2564-35-4 HCAPLUS

CN Guanosine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

RN 39923-67-6 HCAPLUS

CN 5'-Adenylic acid, 2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 39923-68-7 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$NH_2$$
 NH_2
 NH_2

RN 42467-24-3 HCAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2-methyl- (9CI) (CA INDEX NAME)

RN 39923-67-6 HCAPLUS

CN 5'-Adenylic acid, 2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 39923-68-7 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$NH2$$
 $NH2$
 $NH2$

RN 42467-24-3 HCAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2-methyl- (9CI) (CA INDEX NAME)

RN 52940-67-7 HCAPLUS

CN Guanosine 5'-(tetrahydrogen triphosphate), 1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Me N N N O OH OPO3H2
$$R R S$$
 OH OPO3H2
 $R S$ OH OPO3H2

RN 52988-98-4 HCAPLUS

CN Guanosine 5'-(trihydrogen diphosphate), 1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Me N N N N N O P OPO
$$_{3H_2}$$

RN 76528-21-7 HCAPLUS

CN 5'-Cytidylic acid, 5-methoxy- (9CI) (CA INDEX NAME)

RN 80677-38-9 HCAPLUS

CN Cytidine 5'-(trihydrogen diphosphate), 5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 112242-04-3 HCAPLUS

CN Cytidine 5'-(trihydrogen diphosphate), 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 130536-69-5 HCAPLUS

CN Ethanol, 2-(2-iodoethoxy)- (9CI) (CA INDEX NAME)

 $ICH_2 - CH_2 - O - CH_2 - CH_2 - OH$

RN 327174-86-7 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

366451-24-3 HCAPLUS RN

CN Cytidine 5'-(tetrahydrogen triphosphate), 5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

366451-26-5DP, bromide **366451-27-6DP**, bromide **366451-28-7DP**, bromide IT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(fluorescent labeled nucleotide synthesis and application as probes and primers)

RN 366451-26-5 HCAPLUS

3H-Indolium, 5-(aminosulfonyl)-1-(5-carboxypentyl)-2,3,3-trimethyl- (9CI) CN (CA INDEX NAME)

RN 366451-27-6 HCAPLUS

3H-Indolium, 1-(5-carboxypentyl)-5-chloro-2,3,3-trimethyl- (9CI) CN INDEX NAME)

RN 366451-28-7 HCAPLUS

CN 3H-Indolium, 5-chloro-1-[2-(2-hydroxyethoxy)ethyl]-2,3,3-trimethyl- (9CI) (CA INDEX NAME)

$$Me$$
 Me Me $N+$ $CH_2-CH_2-O-CH_2-CH_2-OH$

IT 75-03-6, Ethyl iodide 62306-05-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; fluorescent labeled nucleotide synthesis and application as probes and primers)

RN 75-03-6 HCAPLUS

CN Ethane, iodo- (8CI, 9CI) (CA INDEX NAME)

$$H_3C-CH_2-I$$

RN 62306-05-2 HCAPLUS

CN 3H-Indole-5-sulfonamide, 2,3,3-trimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ H_2N - S & & & \\ \parallel & & & \\ O & & & \\ \end{array}$$

IT 366451-25-4DP, iodide

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(reactant; fluorescent labeled nucleotide synthesis and application as probes and primers)

RN 366451-25-4 HCAPLUS

CN 3H-Indolium, 5-(aminosulfonyl)-1-ethyl-2,3,3-trimethyl- (9CI) (CA INDEX NAME)

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L4
     ANSWER 1 OF 1 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
     2002-151035 [20]
ΑN
                        WPIX
DNN
     N2002-114649
                        DNC C2002-047205
TΙ
     New fluorescent nucleotide, useful for labelling nucleic acids.
DC
     B04 D16 S03
     INOMATA, H; KOJIMA, M; SESHIMOTO, O; SHINOKI, H; SUDO, Y
ΙN
     (FUJF) FUJI PHOTO FILM CO LTD; (INOM-I) INOMATA H; (KOJI-I) KOJIMA M;
PΑ
     (SESH-I) SESHIMOTO O; (SHIN-I) SHINOKI H; (SUDO-I) SUDO Y
CYC
     28
     JP 2001288197
PΙ
                     A 20011016 (200220)*
                                                14
                                                      C07H019-10
                     A2 20011107 (200220) EN
     EP 1152008
                                                      C07H019-06
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     US 2002064782
                     A1 20020530 (200240)
                                                       C12Q001-68
     EP 1152008
                     B1 20050209 (200512) EN
                                                      C07H019-06
         R: DE GB
     DE 60108799
                     E 20050317 (200522)
                                                       C07H019-06
ADT
     JP 2001288197 A JP 2000-107675 20000410; EP 1152008 A2 EP 2001-107864
     20010410; US 2002064782 A1 US 2001-829467 20010409; EP 1152008
     B1 EP 2001-107864 20010410; DE 60108799 E DE 2001-00108799 20010410, EP
     2001-107864 20010410
     DE 60108799 E Based on EP 1152008
PRAI JP 2000-107675
                          20000410
     ICM C07H019-06; C07H019-10; C12Q001-68
         C07H019-16; C07H019-20; C07H021-00; C07H021-04; C09K011-06;
          C12N015-09; C12P019-34; G01N033-53; G01N033-58
     C07D209-08; C07D209-30; C07D403-06; C07D403-14
ICA
AΒ
     JP2001288197 A UPAB: 20020402
     NOVELTY - A new fluorescent nucleotide (I) of the formula A-B-C.
          DETAILED DESCRIPTION - A fluorescent nucleotide of the formula A-B-C
     (I), where:
          A is a residue of natural or synthetic nucleotide, oligonucleotide or
     polynucleotide or their derivatives and combines to B with the base
     portion in the residue, B is a divalent linkage or single bond and C is a
     monovalent group derived from a fluorochrome having water-soluble group
     other than sulfonate group, phosphate group and carboxylic acid group in
     the molecule or a monovalent group derived from a fluorochrome having 0 to
     1 sulfonate or phosphate group in the molecule.
          INDEPENDENT CLAIMS are also included for:
          (1) a method for the preparation of a fluorescence-labelled nucleic
     acid in which a nucleic acid-synthesizing reaction is carried out by using
     a nucleic acid-synthesizing enzyme;
          (2) a template nucleic acid and the above fluorescent nucleotide, a
     nucleic acid probe or primer labelled by the above fluorescent nucleotide,
     a reagent for detecting nucleic acid or a diagnostic agent consisting of
     the above fluorescent nucleotide; and
          (3) a kit for detecting nucleic acid containing:
          (i) the above fluorescent nucleotide;
          (ii) nucleic acid-synthesizing enzyme; and
          (iii) a buffer solution.
          USE - The fluorescent nucleotide is useful for labelling nucleic
     acids.
     Dwg.0/2
ABEX JP 2001288197 AUPTX: 20020402
     EXAMPLE - 1 ml acetonitrile and 2 ml 0.1 M MES buffer were added to 5.75
    mg of the compound of the formula (III) to dissolve it, 2.20 mg WSC
    hydrochloride and 2.52 mg Sulfo-NHS were added to it and stirred at room
     temperature for 30 minutes. 200 microliters 0.1 M MES containing 2.2 mg
```

aminoallyl-deoxyuridine triphosphate was added to it and reacted at room temperature overnight. 100 microliters 1 M Tris buffer was added and the mixture was adsorbed on an ODS silica column and eluted by 30 % aqueous methanol. The eluate was concentrated and purified by a medium pressure preparative chromatography to give the compound of the formula (II).

- KW [1] 93605-0-0-0 CL NEW USE; 105730-0-0-0 CL NEW USE
- FS CPI EPI
- FΑ AB; DCN
- MC CPI: B@4-E01; B04-E05; B04-L01; B11-C08; B11-C08E; B11-C08E5; B12-K04F; D05-H09; D05-H12D; D05-H12D1; D05-H18
 - EPI: S03-E14H
- CMC UPB 20020402
 - M1 *01* M423 M424 M710 M740 M781 M905 N102 N134 N135 P831 Q233 Q505
 - DCN: RA00NS-D; RA00NS-N; RA00NS-U *02* M423 M424 M710 M740 M781 M905 N102 N134 N135 P831 Q233 Q505 Μ1 DCN: RA012P-D; RA012P-N; RA012P-U
 - M6 *03* M905 P831 Q233 Q505 R515 R521 R614 R624 R625 R627 R639

```
=> d his ful
```

L2

L3

L7

```
(FILE 'HOME' ENTERED AT 14:49:06 ON 24 MAR 2006)
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FILE 'HCAPLUS' ENTERED AT 14:49:34 ON 24 MAR 2006 E US2001-829467/APPS

L11 SEA ABB=ON PLU=ON US2001-829467/AP

SEL RN

FILE 'REGISTRY' ENTERED AT 14:49:46 ON 24 MAR 2006

53 SEA ABB=ON PLU=ON (1173-82-6/BI OR 112242-04-3/BI OR 122-51-0/BI OR 130536-69-5/BI OR 14315-97-0/BI OR 146-91-8/BI OR 1927-31-7/BI OR 20309-92-6/BI OR 2056-98-6/BI OR 23065-05-6/ BI OR 2564-35-4/BI OR 25981-83-3/BI OR 327174-86-7/BI OR 3590-36-1/BI OR 365-07-1/BI OR 365-08-2/BI OR 366451-16-3/BI OR 366451-17-4/BI OR 366451-18-5/BI OR 366451-19-6/BI OR 366451-20-9/BI OR 366451-21-0/BI OR 366451-22-1/BI OR 366451-23 -2/BI OR 366451-24-3/BI OR 366451-25-4/BI OR 366451-26-5/BI OR 366451-27-6/BI OR 366451-28-7/BI OR 39923-67-6/BI OR 39923-68-7 /BI OR 4224-70-8/BI OR 42467-24-3/BI OR 491-97-4/BI OR 52940-67-7/BI OR 52988-98-4/BI OR 56-65-5/BI OR 58-64-0/BI OR 58-97-9/BI OR 58-98-0/BI OR 61-19-8/BI OR 62306-05-2/BI OR 628-89-7/BI OR 63-37-6/BI OR 63-38-7/BI OR 63-39-8/BI OR 65-47-4/BI OR 75-03-6/BI OR 76528-21-7/BI OR 80677-38-9/BI OR 85-32-5/BI OR 86-01-1/BI OR 95-50-1/BI)

FILE 'HCAPLUS' ENTERED AT 14:49:59 ON 24 MAR 2006 1 SEA ABB=ON PLU=ON L1 AND L2 D IALL HITSTR

FILE 'WPIX' ENTERED AT 14:50:50 ON 24 MAR 2006 E US2001-829467/AP, PRN

1 SEA ABB=ON PLU=ON US2001-829467/AP L4D MAX

FILE 'HCAPLUS' ENTERED AT 15:00:32 ON 24 MAR 2006 E FLUORESCENT DYE/CT E E4+ALL

L5 9 SEA ABB=ON PLU=ON "FLUORESCENT DYES"+PFT, NT/CT(L)?SULFONAMID?

O SEA ABB=ON PLU=ON L5 AND L1 L6

> FILE 'REGISTRY' ENTERED AT 15:01:57 ON 24 MAR 2006 E ?FLUOR? AND ?DYE? 18 SEA ABB=ON PLU=ON ?FLUOR? AND ?DYE?

FILE 'STNGUIDE' ENTERED AT 15:02:59 ON 24 MAR 2006 FILE 'REGISTRY' ENTERED AT 15:08:01 ON 24 MAR 2006

L8 STR 35 SEA SSS SAM L8 L9 STR L8 L10 20 SEA SSS SAM L10 L11735 SEA SSS FUL L10 L12

L13 3 SEA ABB=ON PLU=ON L12 AND L2 D SCA

6 SEA ABB=ON PLU=ON L12 AND P/ELS L14 D SCA L15 STR

```
L16
               STR L15
L17
             8 SEA SUB=L12 SSS SAM L16
L18
           253 SEA SUB=L12 SSS FUL L16
L19
               STR L16
L20
           227 SEA SUB=L12 SSS FUL L19
L21
               STR L19
L22
              6 SEA SUB=L12 SSS SAM L21
L23
           204 SEA SUB=L12 SSS FUL L21
L24
            49 SEA ABB=ON PLU=ON L18 NOT L23
L25
                STR L21
L26
           213 SEA SUB=L12 SSS FUL L25
L27
            40 SEA ABB=ON PLU=ON L18 NOT L26
L28
             O SEA ABB=ON PLU=ON L26 AND L27
L29
            522 SEA ABB=ON PLU=ON L12 NOT L26
L30
              3 SEA ABB=ON PLU=ON L29 AND L2
                D SCA
              O SEA ABB=ON PLU=ON L26 AND L2
L31
                D QUE L26
                STR L25
L32
                D QUE
L33
                STR L32
L34
               STR L33
L35
             5 SEA SUB=L12 SSS SAM L34
L36
           149 SEA SUB=L12 SSS FUL L34
L37
             O SEA ABB=ON PLU=ON L2 AND L36
            516 SEA ABB=ON PLU=ON L12 NOT (L26 OR L36 OR L14)
L38
             1 SEA ABB=ON PLU=ON L2 AND L38
L39
                D SCA
     FILE 'HCAPLUS' ENTERED AT 15:31:40 ON 24 MAR 2006
L40
           164 SEA ABB=ON PLU=ON L38
L41
              2 SEA ABB=ON PLU=ON L40 AND ?NUCLEOT?
                D SCA
                E NUCLEOTIDES/CT
L42
           5565 SEA ABB=ON PLU=ON NUCLEOTIDES+PFT, NT/CT(L)?FLUOR?
         312511 SEA ABB=ON PLU=ON NUCLEOTIDES+PFT, NT/CT
L43
L44
         70713 SEA ABB=ON PLU=ON OLIGONUCLEOTIDES+PFT, NT/CT
         16053 SEA ABB=ON PLU=ON POLYNUCLEOTIDES+PFT, NT/CT
L45
         738042 SEA ABB=ON PLU=ON (L43 OR L44 OR L45) OR ?NUCLEOTID?
L46
             2 SEA ABB=ON PLU=ON L46 AND L40
L47
L48
          2207 SEA ABB=ON PLU=ON OLIGONUCLEOTIDES+PFT, NT/CT(L)?FLUOR?
L49
           411 SEA ABB=ON PLU=ON POLYNUCLEOTIDES+PFT, NT/CT(L)?FLUOR?
L50
           5565 SEA ABB=ON PLU=ON L42 OR L48 OR L49
                E FLUORESCENT DYES/CT
L51
           5406 SEA ABB=ON PLU=ON FLUORESCENT DYES+PFT, NT/CT
                E CYANINE DYES/CT
L52
          10107 SEA ABB=ON PLU=ON CYANINE DYES+PFT, NT/CT
L53
            303 SEA ABB=ON PLU=ON (L38 OR L51 OR L52) AND L50
                D IBIB ABS HITIND HITSTR
L54
             2 SEA ABB=ON PLU=ON L38 AND L50
L55
             5 SEA ABB=ON PLU=ON L50 AND (L51 OR L52) AND ?SULFONAMID?
L56
             7 SEA ABB=ON PLU=ON L47 OR L54 OR L55
```

FILE HOME

FILE HCAPLUS

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FILE REGISTRY

المحمديد بالم

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 MAR 2006 HIGHEST RN 877759-05-2 DICTIONARY FILE UPDATES: 22 MAR 2006 HIGHEST RN 877759-05-2

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http://www.cas.org/ONLINE/UG/regprops.html

FILE WPIX

FILE LAST UPDATED: 23 MAR 2006 <20060323/UP>
MOST RECENT DERWENT UPDATE: 200620 <200620/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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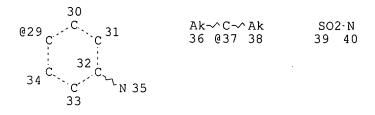
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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que stat L10 STR



VAR G1=0/S/37 VAR G2=12/21/29 NODE ATTRIBUTES: NSPEC IS RC AT 35 DEFAULT MLEVEL IS ATOM GGCAT IS UNS AT 10 DEFAULT ECLEVEL IS LIMITED

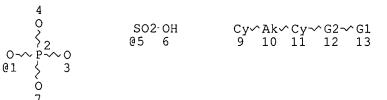
GRAPH ATTRIBUTES:

,, - J.

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 40

STEREO ATTRIBUTES: NONE

L12735 SEA FILE=REGISTRY SSS FUL L10 L14 6 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND P/ELS L25 STR



VAR G1=5/1REP G2 = (0-20) A NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM GGCAT IS UNS AT 10 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L26 213 SEA FILE=REGISTRY SUB=L12 SSS FUL L25

L34 STR 4 O SO2-OH Cy~Ak~Cy~G2~G1 A~A 2 @5 6 9 10 11 12 13 @14 @15 0 7

VAR G1=5/1

., ., 1 *

REP G2=(0-20) 14-11 15-13

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 10
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE										
L36	149	SEA FILE=REGISTRY SUB=L12 SSS FUL L34								
L38	516		26 OR L36 OR L14)							
L40	164		EO ON ESO ON EIT,							
L42		1 1	. DEB NW (CW (T) DET 1100							
1142	5565	SEA FILE=HCAPLUS ABB=ON PLU=ON NUCLEOTIDES ?	+PFT,NT/CT(L)?FLUOR							
L43	312511	SEA FILE=HCAPLUS ABB=ON PLU=ON NUCLEOTIDES	+PFT,NT/CT							
L44	70713	SEA FILE=HCAPLUS ABB=ON PLU=ON OLIGONUCLEO	TIDES+PFT, NT/CT							
L45	16053		IDES+PFT, NT/CT							
L46	738042		OR L45) OR							
?NUCLEOTID?										
L47	2	SEA FILE=HCAPLUS ABB=ON PLU=ON L46 AND L40								
L48	2207		TIDES+PFT, NT/CT(L)?							
		FLUOR?								
L49	411	SEA FILE=HCAPLUS ABB=ON PLU=ON POLYNUCLEOT	IDES+PFT,NT/CT(L)?F							
		LUOR?								
L50	5565	SEA FILE=HCAPLUS ABB=ON PLU=ON L42 OR L48	OR L49							
L51	5406	SEA FILE=HCAPLUS ABB=ON PLU=ON FLUORESCENT	DYES+PFT,NT/CT							
L52	10107		· ·							
L54		SEA FILE=HCAPLUS ABB=ON PLU=ON L38 AND L50	3.1117,117,01							
L55			1 OD 1501 AND							
נכת	5	·	1 OR L52) AND							
	_	?SULFONAMID?								
L56	7	SEA FILE=HCAPLUS ABB=ON PLU=ON L47 OR L54	OR L55							

=> d 156 ibib abs hitind hitstr 1-7

L56 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:610021 HCAPLUS

DOCUMENT NUMBER:

141:153045

TITLE:

Fluorescent assays for screening for protein kinase

inhibitors applicable in cancer treatment and

diagnosis

INVENTOR(S):

Lawrence, David S.

PATENT ASSIGNEE(S):

Albert Einstein College of Medicine of Yeshiva

University, USA

SOURCE:

PCT Int. Appl., 188 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.				KIND		DATE			APPLICATION NO.				DATE				
	WO 2004062475 WO 2004062475				A2 A3		20040729			WO 2004-US480					20040109			
		W:	ΑE,	ΑE,				AM,		AM,	AT,	AT,	AU,	ΑU,	AZ,	AZ,	BA,	BB,
								BY,										
								DE,										
								GD,										
								JP,										
								LS,										
				MX,							•	•		•	•	•		,
US 2005054024				A1		20050310 US 2004-755086						20040109						
PRIORITY APPLN. INFO.:						US 2003-439359					P 20030110							
										1	US 2	003-	5050	97P			0030	

OTHER SOURCE(S):

MARPAT 141:153045

This invention provides fluorescently-labeled peptide substrates for protein kinases; methods using the substrates for identifying compds. that inhibit protein kinases, for determining if particular protein kinases are active in cells, for diagnosing diseases, and for preparing compns.; and compns. comprising the substrates. Several schemes for the synthesis of protein kinase C fluorescently-labeled peptide substrates, adaptable to the preparation of large peptide libraries, are provided. In particular embodiments, a library of fluorescently labeled protein kinase C (PKC) peptide substrates was prepared to identify a phosphorylation-induced reporter of protein kinase activity. The lead PKC substrate displays a 2.5-fold change in fluorescence intensity upon phosphorylation. PKC activity can also be detected in cell lysates containing the activated PKCs and living cells. Immunodepletion of conventional PKCs from the cell lysate eliminates the fluorescence response, suggesting that this peptide substrate is selectively phosphorylated by PKC α , β , and Finally, living cells microinjected with the peptide substrate exhibit a 2-fold increase in fluorescence intensity upon exposure to a PKC. activator. Thus this peptide based protein kinase biosensors is useful in monitoring the temporal and spatial dynamics of PKC activity in living cells, and applicable in cancer treatment and diagnosis.

- IC ICM A61B
- CC 7-3 (Enzymes)

Section cross-reference(s): 1, 9, 13

IT Fluorescent dyes

(Oregon Green conjugated to PKC peptide substrate; fluorescent assays for screening for protein kinase inhibitors applicable in cancer treatment and diagnosis)

IT Alexa

Fluorescent dyes

(conjugated to PKC peptide substrate; fluorescent assays for screening for protein kinase inhibitors applicable in cancer treatment and diagnosis)

IT Fluorescent dyes

(dansyl, conjugated to PKC peptide substrate; fluorescent assays for screening for protein kinase inhibitors applicable in cancer treatment and diagnosis)

IT Amides, biological studies

Amines, biological studies

Esters, biological studies

Ethers, biological studies

Sulfonamides

Thioethers

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(linker, PKC peptide substrate containing; fluorescent assays for screening for protein kinase inhibitors applicable in cancer treatment and diagnosis)

IT **56-65-5**, 5'-ATP, uses

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (used in protein kinase assay; fluorescent assays for screening for protein kinase inhibitors applicable in cancer treatment and diagnosis)

IT **56-65-5**, 5'-ATP, uses

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (used in protein kinase assay; fluorescent assays for screening for protein kinase inhibitors applicable in cancer treatment and diagnosis)

RN 56-65-5 HCAPLUS

Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

L56 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:753071 HCAPLUS

DOCUMENT NUMBER:

135:303873

TITLE:

SOURCE:

Fluorescent labeled nucleotides, synthesis

and application as probes and primers

INVENTOR(S):

Shinoki, Hiroshi; Inomata, Hiroko; Kojima, Masayoshi;

Sudo, Yukio; Seshimoto, Osamu Fuji Photo Film Co., Ltd., Japan Jpn. Kokai Tokkyo Koho, 14 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT ASSIGNEE(S):

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001288197 US 2002064782 EP 1152008 EP 1152008 EP 1152008	A2 A1 A2 A3 B1	20011016 20020530 20011107 20020320 20050209	JP 2000-107675 US 2001-829467 EP 2001-107864	20000410 20010409 20010410
R: AT, BE, CH, IE, SI, LT,		, ES, FR, GE , RO	B, GR, IT, LI, LU, NL,	SE, MC, PT,

```
PRIORITY APPLN. INFO.:
                                             JP 2000-107675
                                                                 A 20000410
OTHER SOURCE(S):
                         MARPAT 135:303873
     The present invention provides a fluorescent substance which is
AB
     represented by a formula: A-B-C wherein A is a residue of natural or
     synthetic nucleotide, oligonucleotide,
     polynucleotide, or derivative thereof, and binds to B at a base moiety
     in said residue; B is a divalent linking group or a single bond; and \tilde{C} is
     a derivative of fluorescent dye having 0 or 1 sulfonate or phosphate moiety.
     Fluorescent dye is cyanine, melocyanine, or styryl. Preferably A is AMP,
     ADP, ATP, GMP, GDP, GTP, CMP, CDP, CTP, UMP, UDP, UTP, TMP, TDP, TTP,
     2-Me-AMP, 2-Me-ADP, 2-Me-ATP, 1-Me-GMP, 1-Me-GDP, 1-Me-GTP, 5-Me-CMP,
     5-Me-CDP, 5-Me-CTP, 5-MeO-CMP, 5-MeO-CDP, 5-MeO-CTP. B is preferably
     -CH2-, -CH=CH-, triple bond, -CO-, -O-, -S-, -NH-, or aminoaryl.
     Synthesis of labeled nucleic acids using the nucleotides via
     reverse transcription, terminal transferase reaction, random prime method,
     PCR, or nick translation, is claimed. The fluorescent substance of the
     present invention is useful as label for nucleic acids, reagent for
     detecting nucleic acids, or diagnostic reagent. Kits for nucleic acid
     detection are claimed. Synthesis of 8 indolenine cyanine compds. and
     conjugation with dUTP, and use for DNA probe preparation, are described.
IC
     ICM C07H019-10
     ICS
          C07H019-20; C07H021-00; C09K011-06; C12N015-09; C12Q001-68;
          G01N033-58; C07D209-08; C07D209-30; C07D403-06; C07D403-14
     28-1 (Heterocyclic Compounds (More Than One Hetero Atom))
CC
     Section cross-reference(s): 3, 9
ST
     fluorescent labeled nucleotide synthesis probe primer; cyanine
     melocyanine styryl nucleotide synthesis probe primer
ΙT
     Diagnosis
        (agents; fluorescent labeled nucleotide synthesis and
        application as probes and primers)
IT
     Phosphates, biological studies
     Sulfonates
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (dye containing; fluorescent labeled nucleotide synthesis and
        application as probes and primers)
     Cyanine dyes
ΙT
     Fluorescent dyes
     Test kits
        (fluorescent labeled nucleotide synthesis and application as
        probes and primers)
IT
     Nucleotides, preparation
       Oligonucleotides
       Polynucleotides
     RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN
     (Synthetic preparation); ANST (Analytical study); BIOL (Biological study);
     PREP (Preparation); USES (Uses)
        (fluorescent labeled nucleotide synthesis and
        application as probes and primers)
ΙT
     Nucleic acid amplification (method)
        (terminal transferase reaction, use in labeled nucleic acid synthesis;
        fluorescent labeled nucleotide synthesis and application as
        probes and primers)
IT
     PCR (polymerase chain reaction)
     Reverse transcription
        (use in labeled nucleic acid synthesis; fluorescent labeled
        nucleotide synthesis and application as probes and primers)
ΙT
     23065-05-6, Styryl
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
```

```
(fluorescent labeled nucleotide synthesis and application as
        probes and primers)
ΙT
     366451-16-3P
                     366451-17-4P 366451-18-5P
                                                  366451-19-6P
     366451-20-9P
                     366451-21-0P
                                    366451-22-1P
                                                    366451-23-2P
     RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN
     (Synthetic preparation); ANST (Analytical study); BIOL (Biological study);
     PREP (Preparation); USES (Uses)
        (fluorescent labeled nucleotide synthesis and application as
        probes and primers)
     56-65-5, 5'-ATP, reactions 58-64-0, 5'-ADP, reactions 58-97-9, 5'-UMP, reactions 58-98-0, 5'-UDP, reactions
ΙT
     61-19-8, 5'-AMP, reactions 63-37-6, CMP 63-38-7
     , CDP 63-39-8, 5'-UTP 65-47-4, 5'-CTP 85-32-5
     , 5'-GMP 86-01-1, 5'-GTP
                                 95-50-1, 1, 2-Dichloro benzene
     122-51-0, Triethyl orthoformate 146-91-8, 5'-GDP
     365-07-1, DTMP 365-08-2, TTP
                                    491-97-4, TDP
     1173-82-6, DUTP 1173-82-6D, DUTP, aminoaryl
     1927-31-7, DATP 2056-98-6, DCTP 2564-35-4,
            3590-36-1
     DGTP
                        4224-70-8, 6-Bromo hexanoic acid
                                                             14315-97-0
     20309-92-6
                  25981-83-3
                                39923-67-6
                                             39923-68-7, 2-Methyl-ADP
     42467-24-3, 2-Methyl-ATP
                                 52940-67-7
                                              52988-98-4
                                                            76528-21-7
     80677-38-9
                 112242-04-3
                                 130536-69-5
                                               327174-86-7
                                                              366451-24-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (fluorescent labeled nucleotide synthesis and
        application as probes and primers)
TΤ
     366451-26-5DP, bromide 366451-27-6DP, bromide
                                                         366451-28-7DP, bromide
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (fluorescent labeled nucleotide synthesis and application as
        probes and primers)
TΤ
     75-03-6, Ethyl iodide
                              62306-05-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reactant; fluorescent labeled nucleotide synthesis and
        application as probes and primers)
IT.
     366451-25-4DP, iodide
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (reactant; fluorescent labeled nucleotide synthesis and
        application as probes and primers)
IT
     366451-18-5P
     RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN
     (Synthetic preparation); ANST (Analytical study); BIOL (Biological study);
     PREP (Preparation); USES (Uses)
        (fluorescent labeled nucleotide synthesis and application as
        probes and primers)
     366451-18-5 HCAPLUS
RN
CN
     3H-Indolium, 5-(aminosulfonyl)-2-[3-[5-(aminosulfonyl)-1-(5-carboxypentyl)-
     1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1-propenyl]-1-ethyl-3,3-
     dimethyl- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

RN 58-64-0 HCAPLUS CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 58-97-9 HCAPLUS CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME) Absolute stereochemistry.

RN 58-98-0 HCAPLUS

CN Uridine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 61-19-8 HCAPLUS

CN 5'-Adenylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 63-37-6 HCAPLUS

CN 5'-Cytidylic acid (8CI, 9CI) (CA INDEX NAME)

RN 63-38-7 HCAPLUS

CN Cytidine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 63-39-8 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 65-47-4 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 85-32-5 HCAPLUS

CN 5'-Guanylic acid (8CI, 9CI) (CA INDEX NAME)

$$H_2N$$
 H_2N
 H_3N
 H_4N
 H_5N
 H_5N
 H_5N
 H_5N
 H_5N
 H_7N
 H_7N

RN 86-01-1 HCAPLUS

CN Guanosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 H_2N
 H_3N
 H_4N
 H_5N
 H_5N
 H_5N
 H_5N
 H_5N
 H_6N
 H_7N
 H_7N

RN 146-91-8 HCAPLUS

CN Guanosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 365-07-1 HCAPLUS

CN 5'-Thymidylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 365-08-2 HCAPLUS

CN Thymidine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 1173-82-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 1173-82-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 1927-31-7 HCAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 2056-98-6 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 2564-35-4 HCAPLUS

CN Guanosine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L56 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:10685 HCAPLUS

DOCUMENT NUMBER: 134:102214

TITLE: New fluorescent cyanine labels containing a

sulfonamido linker arm

INVENTOR(S): Caputo, Giuseppe; Della, Ciana Leopoldo PATENT ASSIGNEE(S): Innosense S.r.L., Italy; Visen Medical, Inc.

SOURCE: Eur. Pat. Appl., 94 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA?	TENT 1	NO.			KINI)	DATE			API	PLI	CAT	ION	NO.		Ε	ATE	
	1065				A1	_		0103		EP	19	99-:	1126	96		1	9990	702
C.F		AT,	BE,	CH,	B1 DE,	DK,	2004 , ES,	FR,	GB,	GF	З, :	IT,	LI,	LU,	NL,	SE,	MC,	PT,
AT	28443		SI,	LT,	LV, E	FI,		1215		АТ	19	99-	1126	96		1	9990	702
EP	1491	591 AT,	ספ	CU	A1	DIZ	2004			ΕP	200	04-2	2314	7		1	9990	702
		IE,	FI,	•	DE,	טת,	, ED,	FR,	GB,	G I	Χ, .	IT,	ы,	LU,	NL,	SE,	MC,	PT,
	77684 23120				B2 AA		2004						1258	_			0000	
	64480				B1		2001						2312: 5090:				0000	
BR PRIORITY	20000				Α		2002	0102					5843				0000	
OTHER SO			TINEO	• •	MARE	PAT	134:	10221	. 4	ĽР	19:	99-1	1126	96	,	A 1	9990	702

AB Water-soluble fluorescent cyanine dyes, capable of being excited by inexpensive light-emitting diodes or diode lasers and of conjugating with a wide variety of biomols., have the structure I [Q = conjugated connecting group; R1, R2 = H, C1-4 (sulfo)alkyl; R3-R5 = H, S03H, C1-4 sulfoalkyl, SO2NH(CH2)mW(CH2)nZ; W = direct link, SO2NH, O, CO2, CONH; X1, X2 = 0, S, CMe2, C:CH2; Y1, Y2 = benzo, naphtho; Z is or contains a functional group capable of bonding to biomols.; m, n = 0-12; m + n = 1-12] or its salt. Thus, K 2,3,3-trimethyl-3H-indole-5-sulfonate was converted with PCl5 and POCl3 to the 5-sulfonyl chloride, which was condensed with glycine tert-Bu ester, and the product was alkylated with 1,4-butane sultone to give 5-[[(carboxymethyl)amino]sulfonyl]-2,3,3trimethyl-1-(4-sulfobutyl)-3H-indolium inner salt (II). 2,3,3-Trimethyl-5-sulfo-1-(4-sulfobutyl)-3H-indolium inner salt was treated first with PhNHCH:NPh and then with II to give a I [Q = CH:CHCH:,R1 = R2 = (CH2)4SO3H; R3 = 5-SO3H, R4 = R5 = H, W = direct link, X1 = X2 =CMe2, Y1 = Y2 = benzo, Z = CO2H, m = 0, n = 1]. IC

Ι

ICM C09B023-02

ICS C07H021-00; C07H019-04; C12Q001-68; G01N033-58

41-6 (Dyes, Organic Pigments, Fluorescent Brighteners, and Photographic CC Sensitizers) Section cross-reference(s): 9

ST fluorescent cyanine dye marker; sulfonamide linker arm fluorescent label

```
ΙT
     Fluorescent dyes
        (cyanine; fluorescent cyanine dye labels containing a sulfonamido
        linker arm)
IT
     Nucleotides, analysis
     RL: ANT (Analyte); ANST (Analytical study)
        (dideoxyribo-; fluorescent cyanine dye labels containing a
        sulfonamido linker arm for)
ΙT
     Immunoassay
        (fluorescence; fluorescent cyanine dye labels containing a
        sulfonamido linker arm for)
ΙT
     Antibodies
       Deoxyribonucleotides
     Nucleosides, analysis
     RL: ANT (Analyte); ANST (Analytical study)
        (fluorescent cyanine dye labels containing a sulfonamido
        linker arm for)
ΙT
     Cyanine dyes
        (fluorescent; fluorescent cyanine dye labels containing a
        sulfonamido linker arm)
IT
     Nucleotides, analysis
     RL: ANT (Analyte); ANST (Analytical study)
        (ribo-; fluorescent cyanine dye labels containing a
        sulfonamido linker arm for)
IT
     115021-69-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (formation of conjugates of fluorescent cyanine dye labels containing a
        sulfonamido linker arm with)
ΙT
                    316829-77-3P
     316829-76-2P
                                   316829-78-4P
                                                   316829-79-5P
                                                                  316829-80-8P
     316829-81-9P 316829-82-0P
                                   316829-83-1P
                                                  316829-84-2P
                                                                  316829-85-3P
     316829-86-4P
                  316829-87-5P
                                   316829-88-6P
                                                  316829-89-7P
                                                                  316829-90-0P
     316829-91-1P
                    316829-92-2P
                                   316829-93-3P
                                                  316829-94-4P
                                                                  316829-95-5P
     316829-96-6P
                    316829-97-7P
                                   316829-99-9P
                                                  316830-00-9P
                                                                  316830-01-0P
     316830-02-1P
                    316830-03-2P
                                   316830-04-3P
                                                  316830-05-4P
                                                                  316830-06-5P
     316830-07-6P
                   316830-08-7P
                                   316830-09-8P
                                                  316830-10-1P
                                                                  316830-11-2P
     316830-13-4P
                   316830-14-5P
                                   316830-15-6P
                                                  316830-16-7P
                                                                  316830-17-8P
     316830-18-9P
                    316830-19-0P
                                   316830-20-3P
                                                  316830-21-4P
                                                                  316830-22-5P
     316830-23-6P
                    316830-24-7P
                                   316830-25-8P
                                                  316830-26-9P
                                                                  316830-27-0P
     316830-28-1P
                    316830-29-2P
                                   316830-30-5P
                                                  316830-31-6P
                                                                  316830-32-7P
     316830-33-8P
                    316830-34-9P
                                   316830-35-0P
                                                  316830-36-1P
                                                                  316830-37-2P
     316830-38-3P
                    316830-39-4P
                                   316830-40-7P
                                                  316830-41-8P
                                                                  316830-42-9P
     316830-43-0P
                    316830-44-1P
                                   316830-45-2P
                                                  316830-46-3P
                                                                  316830-47-4P
     316830-48-5P
                    316830-49-6P
                                   316830-50-9P
                                                  316830-51-0P
                                                                  316830-52-1P
     316830-53-2P
                    316830-54-3P
                                   316830-55-4P
                                                  316830-56-5P
                                                                  316830-57-6P
                    316830-59-8P
     316830-58-7P
                                   316830-60-1P
                                                  316830-61-2P
    RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
     (Analytical study); PREP (Preparation); USES (Uses)
        (preparation of fluorescent cyanine dye labels containing a sulfonamido
        linker arm)
TΤ
    110-60-1, 1,4-Butanediamine
                                   110-87-2, 3,4-Dihydro-2H-pyran
     1,6-Hexanediamine, reactions
                                  407-25-0, Trifluoroacetic anhydride
     622-15-1, N, N'-Diphenylformamidine
                                         1633-83-6, 1,4-Butane sultone
    4048-33-3, 6-Amino-1-hexanol
                                    17576-35-1, 1,3,3-Trimethoxypropene
    33148-94-6
                  58620-93-2
                               58640-01-0, tert-Butyl \gamma-aminobutyrate
    hydrochloride
                    76588-81-3
                                  77284-30-1
                                             184351-56-2, Potassium
    2,3,3-trimethyl-3H-indole-5-sulfonate
                                             316829-43-3, tert-Butyl
    ε-aminocaproate hydrochloride
                                     316829-51-3
                                                   316829-98-8
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of fluorescent cyanine dye labels containing a sulfonamido
        linker arm)
```

```
ΤТ
     316829-38-6P, 2,3,3-Trimethyl-3H-indole-5-sulfonyl chloride
                                                                  316829-39-7P
     316829-40-0P
                   316829-41-1P 316829-42-2P 316829-44-4P,
     N-(4-Aminobuty1)-2,3,3-trimethyl-3H-indole-5-sulfonamide
     316829-45-5P, N-(6-Aminohexyl)-2,3,3-trimethyl-3H-indole-5-
     sulfonamide 316829-46-6P, N-(6-Hydroxyhexyl)-2,3,3-trimethyl-3H-
                          316829-47-7P 316829-48-8P
     indole-5-sulfonamide
     316829-49-9P 316829-50-2P
                                  316829-52-4P
                                                 316829-53-5P
                                                                316829-54-6P
     316829-55-7P 316829-56-8P 316829-57-9P
                                                 316829-58-0P 316829-59-1P
     316829-60-4P 316829-61-5P 316829-62-6P
                                                 316829-63-7P
                                                                316829-64-8P
     316829-65-9P 316829-66-0P 316829-67-1P
                                                 316829-68-2P
                                                                316829-69-3P
     316829-70-6P 316829-71-7P 316829-72-8P 316829-73-9P
                                                                316829-74-0P
     316829-75-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of fluorescent cyanine dye labels containing a sulfonamido
        linker arm)
REFERENCE COUNT:
                        6
                              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L56 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:788697 HCAPLUS
DOCUMENT NUMBER:
                       130:35377
TITLE:
                       Conjugates of sulforhodamine fluorophores with
                        enhanced fluorescence
INVENTOR(S):
                        Kang, Hee Chol
PATENT ASSIGNEE(S):
                     Molecular Probes, Inc., USA
SOURCE:
                       U.S., 18 pp.
                        CODEN: USXXAM
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                 KIND DATE APPLICATION NO. DATE
     PATENT NO.
                        ----
                              -----
                                          -----
                                                                 _____
                        A 19981208 US 1996-686858
     US 5846737
                                                                 19960726
PRIORITY APPLN. INFO.:
                                           US 1996-686858
OTHER SOURCE(S): MARPAT 130:35377
     The invention describes useful conjugates of sulforhodamine, wherein the
     conjugated substance and the fluorophore are separated by an alkanoic acid
     spacer that is attached to the fluorophore via a sulfonamide
     bond. The increased length of the covalent linkage due to the spacer
     results in dye-conjugates having a number of surprisingly advantageous
     properties relative to previous sulforhodamine-labeled conjugates,
    including increased fluorescence. Where the conjugated substance is a member of a specific binding pair, the dye-conjugates possess utility as
     detection reagents for the complementary binding pair member.
IC
     ICM G01N033-533
     ICS C07K016-00; C07D311-88
INCL 435007100
     9-15 (Biochemical Methods)
CC
     Section cross-reference(s): 6
TΤ
    Fluorescent dyes
       (conjugates; conjugates of sulforhodamine fluorophores with enhanced
       fluorescence)
TT
    Nucleotides, analysis
    RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST
     (Analytical study); PREP (Preparation)
        (dideoxynucleotides, dye-conjugates; conjugates of
```

sulforhodamine **fluorophores** with enhanced **fluorescence**)

IT Carbohydrates, analysis

DNA

Lipoproteins

Nucleotides, analysis

Oligonucleotides

Polysaccharides, analysis

RNA

RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)

(dye-conjugates; conjugates of sulforhodamine fluorophores

with enhanced fluorescence)

IT 63-39-8DP, Uridine triphosphate, dye-conjugates

1173-82-6DP, Deoxyuridine triphosphate, dye-conjugates

RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)

(conjugates of sulforhodamine fluorophores with enhanced

fluorescence)

IT 63-39-8DP, Uridine triphosphate, dye-conjugates

1173-82-6DP, Deoxyuridine triphosphate, dye-conjugates

RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)

(conjugates of sulforhodamine fluorophores with enhanced

fluorescence)

RN 63-39-8 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 1173-82-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

2(3H)-benzothiazolylidene]methyl]-2,4-diethyl-1,3,5-octatrienyl]-3-methyl-, chloride (9CI) (CA INDEX NAME)

● cl-

L56 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

1993:170988 HCAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

118:170988

TITLE:

Polymer-bound fluorescent dyes and their use Heiliger, Ludger; Siegmund, Hans Ulrich; Hugel,

Herbert; Loebberding, Antonius; Kuckert, Eberhard; Boemer, Brud; Boecker, Thomas; Franke, Guenter

PATENT ASSIGNEE(S):

SOURCE:

LANGUAGE:

Bayer A.-G., Germany Ger. Offen., 10 pp.

CODEN: GWXXBX

DOCUMENT TYPE:

Patent German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4114482	A1	19921105	DE 1991-4114482	19910503
EP 513560	A1	19921119	EP 1992-106783	19920421
EP 513560	B1	19950920		
R: CH, DE, FR,	GB, IT	, LI, SE		
JP 05230393	A2	19930907	JP 1992-131366	19920427
US 5298583	A	19940329	US 1992-875167	19920428
CA 2067645	AA	19921104	CA 1992-2067645	19920430
PRIORITY APPLN. INFO.:			DE 1991-4114482 A	19910503
AB The dyes, (A)a(B)b(C)c(D)d	, where A is	a water-solubilizing of	group. B is

AB The dyes, (A)a(B)b(C)c(D)d, where A is a water-solubilizing group, B is an ester, amide, urethane, urea, or thiourea group-containing fluorescent mol., C is aromatic or a second fluorescent group, and (D) is a mol. capable of forming a covalent bond with a protein and optionally with component B and(or) C, and a + b + c + d = 100%, are obtained for fluorescent marking

of biol. substances. Thus, a 7-sulfonamido derivative of 3-(4-aminophenyl) coumarin was condensed with acryloyl chloride to provide 85% acrylamide derivative, which could be copolymd. with Na 2-acrylamido-2-propanesulfonate, Na p-styrylsulfonate, and/or 2-naphthyl acrylate.

- IC ICM C09B069-10 ICS C09K011-06; G01N001-30
- ICA C09B057-00; C09B057-02; C09B057-08; C09B003-78; C09B011-12
- CC 41-1 (Dyes, Organic Pigments, Fluorescent Brighteners, and Photographic Sensitizers) Section cross-reference(s): 9, 35
- IT Dyes
- (fluorescent, polymerizable, preparation and application of)
- IT Nucleotides, polymers

RL: USES (Uses)

(oligo-, fluorescent polymeric dyes as labels and
markers for)

- IT 147024-89-3DP, sulfonamido derivative
 - RL: IMF (Industrial manufacture); PREP (Preparation) (preparation and polymerization of fluorescent)
- IT 1218-54-8D, sulfonamido derivative 131788-68-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with acryloyl chloride)

```
=> d que stat
L1
          26778 SEA FILE=WPIX ABB=ON PLU=ON B04-E01/MC
L2
          21339 SEA FILE=WPIX ABB=ON PLU=ON B04-E05/MC
L3
           7416 SEA FILE=WPIX ABB=ON PLU=ON L1 AND L2
          20421 SEA FILE=WPIX ABB=ON PLU=ON B11-C08E5/MC
L5
L6
           5578 SEA FILE=WPIX ABB=ON PLU=ON L3 AND L5
          26902 SEA FILE=WPIX ABB=ON PLU=ON B12-K04F/MC 5039 SEA FILE=WPIX ABB=ON PLU=ON L6 AND L7
L7
L11
           1177 SEA FILE=WPIX ABB=ON PLU=ON L8 AND ?FLUORES?
L12
           845 SEA FILE=WPIX ABB=ON PLU=ON L11 AND ?NUCLEOTID?
              6 SEA FILE=WPIX ABB=ON PLU=ON L12 AND ?SULFONAMID?
L13
              6 SEA FILE-WPIX ABB-ON PLU-ON L13 AND (DYE? OR ?LABEL? OR
L14
                ?PROB? OR PRIMER?)
=> d l14 ibib ab's kwic 1-6
L14 ANSWER 1 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER:
                      2004-130831 [13]
                                          WPIX
                      2001-007201 [01]; 2002-075152 [10]; 2003-129427 [12];
CROSS REFERENCE:
                      2003-182493 [18]; 2003-183881 [18]; 2003-237970 [23];
                      2003-505116 [47]; 2003-597938 [56]; 2003-617918 [58];
                      2003-777244 [73]; 2003-800810 [75]; 2003-842577 [78];
                      2003-843672 [78]; 2004-070573 [07]; 2004-118571 [12];
                      2004-156863 [15]; 2004-294400 [27]; 2004-614756 [59];
                      2004-718458 [70]; 2004-737692 [72]; 2004-766859 [75];
                      2004-821135 [81]; 2004-821145 [81]; 2005-012615 [01];
                      2005-056557 [06]; 2005-130051 [14]; 2005-202666 [21]; 2005-212277 [22]; 2005-315587 [32]; 2005-344285 [35];
                      2005-443802 [45]; 2005-562735 [57]; 2005-562736 [57]
DOC. NO. CPI:
                      C2004-052186
TITLE:
                      Detecting and/or measuring multiple analytes in sample by
                      nucleic acid based signal amplification system for
                      simultaneous generation of multiple molecular tags.
DERWENT CLASS:
                      B04 C07 D16
INVENTOR(S):
                      MACEVICZ, S C; MATRAY, T; SINGH, S; MATRAY, T J; SINGH, S
PATENT ASSIGNEE(S):
                      (ACLA-N) ACLARA BIOSCIENCES INC; (MACE-I) MACEVICZ S C;
                      (MATR-I) MATRAY T J; (SING-I) SINGH S S
COUNTRY COUNT:
                      102
PATENT INFORMATION:
     PATENT NO
                   KIND DATE
                                         LA PG
                                   WEEK
     US 2003207300 A1 20031106 (200413)*
                                                66
     WO 2004063700 A2 20040729 (200451) EN
        RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
            LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
            RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
    AU 2003296989
                   A1 20040810 (200479)
    EP 1581796
                     A2 20051005 (200565)
                                            EN
         R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
            MC MK NL PT RO SE SI SK TR
```

APPLICATION DETAILS:

		Fredman	09/829,461	DATE
DATENT NO	ND A1 CIP of CIP of CIP of		APPLICATION US 2000-561579 US 2000-602586 US 2000-698846 US 2002-154042 US 2003-338729 US 2003-339613	20000428 20000621 20001027 20020521 20030107 20031212 20031212 20031212
WO 2004063700 AU 2003296989 EP 1581796	A2 A1 A2		WO 2003-000989 AU 2003-296989 EP 2003-815205 WO 2003-US39613	20031212

EP 1581/96			
FILING DETAILS:		PATENT NO	
PATENT NO US 200320730 AU 200329698 EP 1581796 PRIORITY APPLN.	A2 Based 33 INFO: US 2003-338729 2000-561579 2000-602586 2000-698846 2002-154042	20020521	12]; 2003-182493 [18]; 47]; 2003-597938 [56];
AN 2004-13083 2001-00720 2003-18380 2003-6179 2003-8436 2004-2944 2004-7660 2005-056 2005-315 2005-562	11 [01]; 2002-03-237970 12 [18]; 2003-237970 13 [58]; 2003-777244 14 [58]; 2004-070573 15 [78]; 2004-614756 15 [75]; 2004-821135 15 [75]; 2004-821135	[23]; 2003-800810 [73]; 2004-118571 [07]; 2004-718458 [59]; 2004-821145 [81]; 2005-202666 [14]; 2005-443802	[12]; 2004-156863 [72]; [70]; 2004-737692 [72]; [70]; 2005-012615 [01]; [81]; 2005-212277 [22]; [21]; 2005-562735 [57];

US2003207300 A UPAB: 20051011 AB

NOVELTY - Generating (M1) molecular tags (MT) indicative of several of polynucleotides (PN) in sample, comprising extending

polynucleoliues (FN) in sample, complianting on the DP)
primer annealed to each PN to form detection probe (DP)

having MT and either a sensitizer or a capture moiety, generating detectable amounts of DP, activating sensitizers to generate active species that cleaves the linkages, thus releasing MT, and separating and identifying released MT is now

DETAILED DESCRIPTION - Generating (M1) molecular tags indicative of identifying released MT, is new.

several polynucleotides in a sample, comprising:

(a) extending a primer annealed to each

conditions that permit dissociation of detection probes from the polynucleotide to form a detection probe under having a molecular tag and either a sensitizer with an effective proximity polynucleotides after extension, each detection probe or a capture moiety, the molecular tag being attached by a cleavable linkage and within the effective proximity of the sensitizer upon

attached, and the molecular tag being chosen from several molecular tags polynucleotide when the detection probe has a sensitizer dissociation of the detection probe from the so that each molecular tag has one or more physical and/or optical so that each morecular tay has one or more physical and/or opercal characteristics distinct from those of the other molecular tags so that each molecular tag forms a distinguishable peak upon cleavage and separation based on one or more physical and/or optical characteristics;

```
=> d que stat
L1
          26778 SEA FILE=WPIX ABB=ON PLU=ON B04-E01/MC
          21339 SEA FILE=WPIX ABB=ON PLU=ON B04-E05/MC
L2
L3
           7416 SEA FILE-WPIX ABB-ON PLU-ON L1 AND L2
L5
          20421 SEA FILE=WPIX ABB=ON PLU=ON B11-C08E5/MC
L6
          5578 SEA FILE=WPIX ABB=ON PLU=ON L3 AND L5
L7
          26902 SEA FILE=WPIX ABB=ON PLU=ON B12-K04F/MC
L8
          5039 SEA FILE=WPIX ABB=ON PLU=ON L6 AND L7
L11
          1177 SEA FILE-WPIX ABB-ON PLU-ON L8 AND ?FLUORES?
L12
          845 SEA FILE=WPIX ABB=ON PLU=ON L11 AND ?NUCLEOTID?
             6 SEA FILE=WPIX ABB=ON PLU=ON L12 AND ?SULFONAMID?
L13
L14
              6 SEA FILE=WPIX ABB=ON PLU=ON L13 AND (DYE? OR ?LABEL? OR
                ?PROB? OR PRIMER?)
=> d l14 ibib ab's kwic 1-6
L14 ANSWER 1 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER:
                     2004-130831 [13]
                                       WPTX
CROSS REFERENCE:
                     2001-007201 [01]; 2002-075152 [10]; 2003-129427 [12];
                     2003-182493 [18]; 2003-183881 [18]; 2003-237970 [23];
                     2003-505116 [47]; 2003-597938 [56]; 2003-617918 [58];
                     2003-777244 [73]; 2003-800810 [75]; 2003-842577 [78];
                     2003-843672 [78]; 2004-070573 [07]; 2004-118571 [12];
                     2004-156863 [15]; 2004-294400 [27]; 2004-614756 [59];
                     2004-718458 [70]; 2004-737692 [72]; 2004-766859 [75];
                     2004-821135 [81]; 2004-821145 [81]; 2005-012615 [01];
                     2005-056557 [06]; 2005-130051 [14]; 2005-202666 [21];
                     2005-212277 [22]; 2005-315587 [32]; 2005-344285 [35];
                     2005-443802 [45]; 2005-562735 [57]; 2005-562736 [57]
DOC. NO. CPI:
                     C2004-052186
TITLE:
                     Detecting and/or measuring multiple analytes in sample by
                     nucleic acid based signal amplification system for
                     simultaneous generation of multiple molecular tags.
DERWENT CLASS:
                     B04 C07 D16
INVENTOR(S):
                     MACEVICZ, S C; MATRAY, T; SINGH, S; MATRAY, T J; SINGH, S
PATENT ASSIGNEE(S):
                     (ACLA-N) ACLARA BIOSCIENCES INC; (MACE-I) MACEVICZ S C;
                     (MATR-I) MATRAY T J; (SING-I) SINGH S S
COUNTRY COUNT:
                     102
PATENT INFORMATION:
    PATENT NO
                  KIND DATE WEEK
                                          LA PG
    ______
    US 2003207300 A1 20031106 (200413) * 66
    WO 2004063700 A2 20040729 (200451) EN
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           LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
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           DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
           KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
           RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
    AU 2003296989 A1 20040810 (200479)
    EP 1581796
                   A2 20051005 (200565)
                                         ΕN
        R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
           MC MK NL PT RO SE SI SK TR
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APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003207300	A1 CIP of CIP of CIP of CIP of	US 2000-561579 US 2000-602586 US 2000-698846 US 2002-154042 US 2003-338729	20000428 20000621 20001027 20020521 20030107
WO 2004063700 AU 2003296989 EP 1581796	A2 A1 A2	WO 2003-US39613 AU 2003-296989 EP 2003-815205 WO 2003-US39613	20031212 20031212 20031212 20031212

FILING DETAILS:

I	PATENT NO	KIND	PATENT NO	
7	AU 2003296989	Al CIP of Al Based on A2 Based on	WO 200406370	0000
PRIOR	ITY APPLN. INFO	: US 2003-338729 2000-561579 2000-602586 2000-698846 2002-154042	20000428; US 20000621; US 20001027; US	US
CR	2003-183881 [18 2003-617918 [58 2003-843672 [78 2004-294400 [27 2004-766859 [75 2005-056557 [06]; 2002-075152 [10]; 2003-237970 [23]; 2003-777244 [73]; 2004-070573 [03]; 2004-614756 [53]; 2004-821135 [83]; 2005-130051 [14]; 2005-344285 [33]	3]; 2003-505116 3]; 2003-800810 7]; 2004-118571 9]; 2004-718458 1]; 2004-821145 4]; 2005-202666	[12]; 2003-182493 [18]; [47]; 2003-597938 [56]; [75]; 2003-842577 [78]; [12]; 2004-156863 [15]; [70]; 2004-737692 [72]; [81]; 2005-012615 [01]; [21]; 2005-212277 [22]; [45]; 2005-562735 [57];
	polynucleotides primer annealed having MT and e detectable amou species that cl identifying rel	ating (M1) molecu (PN) in sample, to each PN to fo ither a sensitize nts of DP, activa eaves the linkage eased MT, is new.	comprising exter rm detection pro r or a capture n ting sensitizers s, thus releasing	ndicative of several of nding bbe (DP) moiety, generating s to generate active ng MT, and separating and ecular tags indicative of

DETAILED DESCRIPTION - Generating (M1) molecular tags indicative of several polynucleotides in a sample, comprising:

(a) extending a primer annealed to each polynucleotide to form a detection probe under conditions that permit dissociation of detection probes from the polynucleotides after extension, each detection probe having a molecular tag and either a sensitizer with an effective proximity or a capture moiety, the molecular tag being attached by a cleavable linkage and within the effective proximity of the sensitizer upon dissociation of the detection probe from the polynucleotide when the detection probe has a sensitizer attached, and the molecular tag being chosen from several molecular tags so that each molecular tag has one or more physical and/or optical characteristics distinct from those of the other molecular tags so that each molecular tag forms a distinguishable peak upon cleavage and separation based on one or more physical and/or optical characteristics;

- (b) generating detectable amounts of detection **probes** in the step of extending, activating the sensitizers to generate an active species so that the cleavable linkages are cleaved and the molecular tags are released; and
- (c) separating and identifying the released molecular tags to determine several **polynucleotides** in the sample.

An INDEPENDENT CLAIM is also included for a composition (C) of matter having formula (I) or (II), or comprising one or more photosensitizer beads having a complementary moiety attached, the complementary moiety capable of capturing a capture moiety, and one or more oligonucleotides each having attached a capture moiety and a molecular tag, the molecular tag attached by a cleavable linkage, and each molecular tag chosen from several molecular tags such that each molecular tag has one or more physical and/or optical characteristics distinct from those of the other molecular tags such that each molecular tag forms a distinguishable peak upon cleavage and separation based on one or more physical and/or optical characteristics, where each of the one or more oligonucleotides are attached to the one or more photosensitizer beads by specific binding of the capture moiety to the complementary moiety.

B = nucleobase;

R1 = OH, mono- or di- triphosphate, or its analog;

R2 = -OH, H, F, C1, NH2, N3, or OR';

R3 = -OH, H, F, C1, NH2, N3 or OR';

R' = 1-6C alkyl;

L = cleavable linkage;

L' = diradical moiety of 1-50 atoms chosen from hydrogen, carbon, oxygen, nitrogen, phosphorous and sulfur;

PS = photosensitizer;

D = detection moiety; and

 ${\rm M}={\rm a}$ bond or a water soluble organic compound consisting of 1-100 atoms, not including hydrogen, chosen from carbon, oxygen, nitrogen, phosphorous, boron, sulfur.

USE - (M1) is useful for generating molecular tags indicative of several of polynucleotides in a sample (claimed).

ADVANTAGE - (M1) exhibits greater sensitivity, convenient multiplexing capability, and reduced background.

DESCRIPTION OF DRAWING(S) - The drawing shows generation of reaction **probes** with a polymerase that extends a molecular taglabeled primer by a single nucleotide having a photosensitizer attached.

Dwg.1A/11

AB

US2003207300 UPAB: 20051011

NOVELTY - Generating (M1) molecular tags (MT) indicative of several of polynucleotides (PN) in sample, comprising extending primer annealed to each PN to form detection probe (DP) having MT and either a sensitizer or a capture moiety, generating detectable amounts of DP, activating sensitizers to generate. . . releasing MT, and separating and identifying released MT, is new.

DETAILED DESCRIPTION - Generating (M1) molecular tags indicative of several polynucleotides in a sample, comprising:

(a) extending a primer annealed to each polynucleotide to form a detection probe under conditions that permit dissociation of detection probes from the polynucleotides after extension, each detection probe having a molecular tag and either a sensitizer with an effective proximity or a capture moiety, the molecular tag being attached by a cleavable linkage and within the effective proximity of the sensitizer upon dissociation of the detection probe from the

polynucleotide when the detection probe has a sensitizer
attached, and the molecular tag being chosen from several molecular tags
so that each molecular tag has. . . peak upon cleavage and separation
based on one or more physical and/or optical characteristics;

- (b) generating detectable amounts of detection **probes** in the step of extending, activating the sensitizers to generate an active species so that the cleavable linkages are cleaved and the molecular tags are released; and
- (c) separating and identifying the released molecular tags to determine several **polynucleotides** in the sample.

An INDEPENDENT CLAIM is also included for a composition (C) of matter having formula (I) or (II),. . . photosensitizer beads having a complementary moiety attached, the complementary moiety capable of capturing a capture moiety, and one or more oligonucleotides each having attached a capture moiety and a molecular tag, the molecular tag attached by a cleavable linkage, and each. . . upon cleavage and separation based on one or more physical and/or optical characteristics, where each of the one or more oligonucleotides are attached to the one or more photosensitizer beads by specific binding of the capture moiety to the complementary moiety. . . from carbon, oxygen, nitrogen, phosphorous, boron, sulfur.

USE - (M1) is useful for generating molecular tags indicative of several of **polynucleotides** in a sample (claimed).

ADVANTAGE - (M1) exhibits greater sensitivity, convenient multiplexing capability, and reduced background.

DESCRIPTION OF DRAWING(S) - The drawing shows generation of reaction probes with a polymerase that extends a molecular tag-labeled primer by a single nucleotide having a photosensitizer attached.

Dwg.1A/11

TECH.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M1), the step of extending includes extending with a DNA polymerase the **primer** by a terminator, the terminator having the sensitizer attached or the capture moiety attached. The terminator has the capture moiety attached, and where after the step of generating detectable amounts of the detection **probes**, a further step of capturing each of the detection **probes** by a complementary moiety of the capture moiety, the complementary moiety being attached to a photosensitizer bead. The capture moiety. . . D are as described above. The several molecular tags is in the range of 2-100, and where D is a **fluorescent label**

Preferred Composition: In (C), L is chosen from olefins, thioethers, selenoethers, thiazoles, oxazoles, and imidazoles having 6-100 atoms, not including hydrogen, chosen from carbon, oxygen, nitrogen, phosphorus, boron, and sulfur. D is a fluorescent, a chromogenic, or an electrochemical label. M is a polymer chosen from polyethers, polyesters, polypeptides, oligosaccharides, polyurethanes, polyamides, polysulfonamides, polysulfoxides, polyphosphonates, and its block copolymers. Preferably, D is a fluorescein which is chosen from 5- and 6-carboxyfluorescein, 5- and 6-carboxy-4,7-dichlorofluorescein, 2'-7'-dimethoxy-5- and 6-carboxy-4,7-dichlorofluorescein, 2',7'-dimethoxy-4',5'-dichloro-5- and 6-carboxy-4,7-dichlorofluorescein. L is chosen from olefins, thioethers, selenoethers, thiazoles, oxazoles, and imidazoles. The molecular tags is in the range of from. . .

MC CPI: B04-B03; B04-E01; B04-E05; B11-C08E5; B12-K04F; C04-B03; C04-E01; C04-E05; C11-C08E5; C12-K04F;

D05-A02B; D05-H09; D05-H12D1; D05-H18B

L14 ANSWER 2 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: DOC. NO. CPI:

2003-039601 [03] WPIX

DOC. N

C2003-009343

TITLE:

Novel polymorphisms of N-acetyltransferase 2 gene

involved in drug metabolism and various disorders useful

in therapeutics and to identify polymorphisms as a

predisposition to various diseases e.g. cancer, leprosy.

DERWENT CLASS: B04 D16

INVENTOR(S):

FITZGERALD, M; THOMANN, H; WALL, K

PATENT ASSIGNEE(S):

(FITZ-I) FITZGERALD M; (THOM-I) THOMANN H; (WALL-I) WALL

K 1

COUNTRY COUNT:

PATENT INFORMATION:

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002128215	Al Provisional	US 2000-179876P US 2001-776407	20000202

PRIORITY APPLN. INFO: US 2000-179876P

20000202; US

2001-776407

20010202

AN 2003-039601 [03] WPIX

AB US2002128215 A UPAB: 20030113

NOVELTY - An isolated nucleic acid (I) comprising at least 15 consecutive ${\bf nucleotide}$ bases including a polymorphic site in the wild type N-acetyltransferase 2 (NAT-2) gene, is new.

DETAILED DESCRIPTION - An isolated nucleic acid (I) comprising at least 15 consecutive **nucleotide** bases including a polymorphic site in the wild type N-acetyltransferase 2 (NAT-2) gene, is new.

- (I) comprises at least 15 consecutive nucleotide bases including a polymorphic site chosen from C to G substitution at nucleotide -255, 403 or 51, C to T substitution at nucleotide -234, a T to A substitution at nucleotide 70, G to T substitution at nucleotide 609 and a G to A substitution at nucleotide 838 in the wild type NAT-2 gene which has a sequence (S1) of 1170 bp given in the specification.
 - INDEPENDENT CLAIMS are included for the following:
- (1) an isolated allele specific primer (II) capable of detecting a polymorphic site of (S1);
- (2) an isolated allele specific oligonucleotide
 probe (III) capable of detecting a polymorphic site of (S1);
 - (3) a diagnostic kit (IV) comprising (II) or (III);
- (4) an isolated nucleic acid (V) comprising at least 50 consecutive nucleic acids of (S1) containing at least one of the polymorphic sites as above;
 - (5) an expression vector (VI) containing (I) or (V);
 - (6) a host cell (VII) containing (VI);
- (7) an isolated polypeptide (VIII) comprising at least 5 consecutive amino acid bases, one or more of which are encoded by the nucleotides at a polymorphic site of (I) or its complement;

- (8) an isolated polypeptide (IX) comprising at least 5 consecutive amino acid bases including a polymorphic site chosen from a Asn to substitution at amino acid position 17, a Leu to Ile substitution at position 24, a Leu to Val substitution at position 135, a Glu to Asp substitution at position 203, and a Val to Met substitution at position 280 of a sequence (S2) of 291 amino acids given in the specification;
 - (9) an isolated amino acid sequence (X) having 80% identity to (IX);
- (10) an antibody (XI) or its fragment which binds to any of the above polypeptide sequences;
- (11) an antisense oligonucleotide (XII) comprising at least
 5 nucleotide bases of a polymorphic site of (I);
- (12) detecting (M1) (I), by a method chosen from restriction fragment length polymorphism detection based on allele specific restriction endonuclease cleavage, hybridization with allele specific oligonucleotide probes, oligonucleotide
- arrays, allele specific polymerase chain reaction (PCR), mismatch repair detection (MRD), denaturing gradient gel electrophoresis (DGGE), single strand conformation polymorphism detection (SSCP), RNAase cleavage at mismatched bp chemical or cleavage of heteroduplex DNA, methods based on allele specific primer extension, genetic bit analysis (GBA), oligonucleotide ligation assay (OLA), allele specific ligation chain reaction (LCR), gap, radioactive and/or fluorescent DNA sequencing, and peptide nucleic acid (PNA) assays;
- (13) identifying (M2) a polymorphism of (I) in a mammal, by preparing a sample of cells or tissue of the mammal, **probing** the tissue or cell with all or a portion of a polymorphism of (I) under conditions where hybridized DNA can be produced, identifying the hybridized DNA and cloning and sequencing the hybridized DNA to obtain and identify the NAT-2 gene in the mammal;
- (14) treating (M3) a NAT-2 disorder by administering a molecule which binds to an endogenous analog of NAT-2 or a compound which is an agonist or antagonist of (I), its variant or fragment;
- (15) **labeling** (M4) an individual in a clinical trial, by producing a library of SNPs including the polymorphic sites of (I) and their respective phenotype, sequencing an individuals NAT-2 gene, matching the genotype with the phenotype;
- (16) creating (M5) a prognosis protocol by identifying patients receiving at least one NAT-2 drug, determining whether they are rapid acetylator or a slow acetylator, and converting the data obtained into a prognosis protocol;
- (17) identifying (M6) therapeutic compositions which are efficacious in individuals, by administering a therapeutic composition to an individual and measuring its efficacy, determining by the individual's genotype and the polymorphic sites of (I) whether the individual is a rapid acetylator and slow acetylator, and determining which therapeutic composition will be the most effective for that particular genotype and which will have the least adverse effects;
- (18) identifying (M7) an individual, by sequencing an individual's NAT-2 gene, comparing the results the frequency of NAT-2 in the population as given in the specification, using the data with other polymorphic sites in the human genome to statistically conclude the likelihood of the set of SNPs from this individual as compared to the general population;
- (19) genetically linking (M8) a first individual to a second individual, by sequencing the NAT-2 gene of the first individual and parents of the second individual, comparing the particular SNPs from the two parents with the SNPs of the second individual, matching SNPs of the parents of the second individual and assessing, through statistical methods utilizing the frequency given in the specification, the likelihood of this frequency of SNPs in the general population; and

(20) a computer readable medium (XIII) comprising (I).

ACTIVITY - Cytostatic; Antileprotic. No biological data given. MECHANISM OF ACTION - Gene therapy; Modulator of (I). USE - (I) is useful for diagnosis and gene therapy, to identify DNA probes for NAT-2 genes, PCR primers to amplify NAT-2 genes and regulatory elements of the NAT-2 genes. (I) is useful for identifying individuals and in paternity testing. (I) is useful as a valuable information source to characterize individuals in terms of haplotypes and other sub-groupings, such as investigation of susceptibility to treatment with particular drugs. The polynucleotide sequences are particularly useful as components in databases useful for sequence identity and other search analyses. (IX) is useful as an immunogen to generate antibody that binds the polymorphic protein, and for screening for drugs. (M3) is useful for treating NAT-2 disorders such as bladder cancer, colon cancer, prostate cancer, Gilbert's disease and leprosy. (I) is useful in diagnosing individuals with NAT-2 polymorphisms which are associated with these diseases and affect the metabolism of the compounds. (M5) is useful for creating a prognosis protocol for a patient receiving a therapeutic composition metabolized by NAT-2 such as isoniazid, phenylzine, hydrazine, dapsone, procainamide, sulfamethazine and other sulfonamides. The prognosis protocol includes prediction of drug efficacy, prediction of patient's prognosis, prediction of drug interaction and prediction of adverse effects. Cells and animals that carry the NAT-2 gene or its analog are useful as model systems to study and test for substances that have potential as therapeutic agents.

Dwg.0/2 AB US20021

US2002128215 UPAB: 20030113

NOVELTY - An isolated nucleic acid (I) comprising at least 15 consecutive **nucleotide** bases including a polymorphic site in the wild type N-acetyltransferase 2 (NAT-2) gene, is new.

DETAILED DESCRIPTION - An isolated nucleic acid (I) comprising at least 15 consecutive **nucleotide** bases including a polymorphic site in the wild type N-acetyltransferase 2 (NAT-2) gene, is new.

- (I) comprises at least 15 consecutive nucleotide bases including a polymorphic site chosen from C to G substitution at nucleotide -255, 403 or 51, C to T substitution at nucleotide -234, a T to A substitution at nucleotide 70, G to T substitution at nucleotide 609 and a G to A substitution at nucleotide 838 in the wild type NAT-2 gene which has a sequence (S1) of 1170 bp given in the specification.
 - INDEPENDENT CLAIMS are included for the following:
- (1) an isolated allele specific primer (II) capable of detecting a polymorphic site of (S1);
- (2) an isolated allele specific oligonucleotide
 probe (III) capable of detecting a polymorphic site of (S1);
- (3) a diagnostic kit (IV) comprising (II) or (III);
 . . isolated polypeptide (VIII) comprising at least 5 consecutive amino acid bases, one or more of which are encoded by the nucleotides at a polymorphic site of (I) or its complement;
- (8) an isolated polypeptide (IX) comprising at least 5 consecutive amino. . (10) an antibody (XI) or its fragment which binds to any of the above polypeptide sequences;
- (11) an antisense oligonucleotide (XII) comprising at least 5 nucleotide bases of a polymorphic site of (I);
- (12) detecting (M1) (I), by a method chosen from restriction fragment length polymorphism detection based on allele specific restriction endonuclease cleavage, hybridization with allele specific oligonucleotide probes, oligonucleotide

arrays, allele specific polymerase chain reaction (PCR), mismatch repair detection (MRD), denaturing gradient gel electrophoresis (DGGE), single strand conformation polymorphism detection (SSCP), RNAase cleavage at mismatched bp chemical or cleavage of heteroduplex DNA, methods based on allele specific primer extension, genetic bit analysis (GBA), oligonucleotide ligation assay (OLA), allele specific ligation chain reaction (LCR), gap, radioactive and/or fluorescent DNA sequencing, and peptide nucleic acid (PNA) assays; (13) identifying (M2) a polymorphism of (I) in a mammal, by preparing a sample of cells or tissue of the mammal, probing the tissue or cell with all or a portion of a polymorphism of (I) under conditions where hybridized DNA can. . . analog of NAT-2 or a compound which is an agonist or antagonist of (I), its variant or fragment; (15) labeling (M4) an individual in a clinical trial, by producing a library of SNPs including the polymorphic sites of (I) and. - Gene therapy; Modulator of (I). USE - (I) is useful for diagnosis and gene therapy, to identify DNA probes for NAT-2 genes, PCR primers to amplify NAT-2 genes and regulatory elements of the NAT-2 genes. (I) is useful for identifying individuals and in paternity. . . characterize individuals in terms of haplotypes and other sub-groupings, such as investigation of susceptibility to treatment with particular drugs. The polynucleotide sequences are particularly useful as components in databases useful for sequence identity and other search analyses. (IX) is useful as. . . for a patient receiving a therapeutic composition metabolized by NAT-2 such as isoniazid, phenylzine, hydrazine, dapsone, procainamide, sulfamethazine and other sulfonamides. The prognosis protocol includes prediction of drug efficacy, prediction of patient's prognosis, prediction of drug interaction and prediction of adverse. CPI: B04-B03C; B04-C01A; B04-C01B; B04-C01C; B04-C01D; B04-C01E; B04-C01F; B04-C01G; B04-E01; B04-E02F; B04-E05; B04-E06; B04-E08; B04-E09; B04-E10; B04-F0100E; B04-G01; B04-L04; B04-N04B0E; B11-C07B3; B11-C07B5; B11-C08D1; B11-C08E2; B11-C08E3; B11-C08E4; B11-C08E5; B11-C08F1; B11-C08F2; B11-C10; B12-K04A; B12-K04E; B12-K04F; B14-A01B1; B14-H01; B14-L01; B14-L06; B14-S03; D05-C11; D05-H09; D05-H11; D05-H12A; D05-H12D1; D05-H12D2; D05-H12E; D05-H14; D05-H16A; D05-H17A6 L14 ANSWER 3 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN ACCESSION NUMBER: 2001-104835 [12] WPIX CROSS REFERENCE: 2005-067563 [08] DOC. NO. NON-CPI: N2001-077759 DOC. NO. CPI: C2001-030929 TITLE: New fluorescent cyanine labels containing sulfonamido linker. DERWENT CLASS: B04 D16 E13 E23 S03 INVENTOR(S): CAPUTO, G; CIANA, L D; DELLA CIANA, L; DELLA, C L PATENT ASSIGNEE(S): (INNO-N) INNOSENSE SRL; (VISE-N) VISEN MEDICAL INC COUNTRY COUNT: 29 PATENT INFORMATION: PATENT NO KIND DATE WEEK T.A -----EP 1065250 A1 20010103 (200112) * EN R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

MC

RO SE SI

AU 2000042581

CA 2312099

A 20010111 (200112)

A1 20010102 (200114)

BR	2000005843	Α	20020102	(200206)								
US	6448008	В1	20020910	(200263)								
ΑU	776841	В2	20040923	(200480)								
EΡ	1065250	В1	20041208	(200480)	EN							
	R: AT BE CH	CY	DE DK ES	FI FR GB	GR IE	ΙT	LI	LU	MC	NL	PT	SE
DΕ	69922498	Ε	20050113	(200506)								
DΕ	69922498	Т2	20051208	(200581)								

APPLICATION DETAILS:

PAT	ENT NO	KIND)	Al	PPLICATION	DATE
ΕP	1065250	- -		EP	1999-112696	19990702
ΑU	2000042581	Α		AU	2000-42581	20000621
CA	2312099	A1		CA	2000-2312099	20000622
BR	2000005843	Α		BR	2000-5843	20000703
US	6448008	В1		US	2000-609035	20000630
ΑU	776841	B2		AU	2000-42581	20000621
ΕP	1065250	В1		EP	1999-112696	19990702
			Related	to EP	2004-23147	19990702
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				EP	1999-112696	19990702
DE	69922498	Т2		DE	1999-622498	19990702
				EP	1999-112696	19990702

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 776841 DE 69922498	B2 Previous Publ.	AU 2000042581
DE 69922498	E Based on T2 Based on	EP 1065250 EP 1065250

PRIORITY APPLN. INFO: EP 1999-112696 19990702; EP 2004-23147 19990702

AN 2001-104835 [12] WPIX

CR 2005-067563 [08]

AB EP 1065250 A UPAB: 20051216

NOVELTY - Fluorescent cyanine labels containing a sulfonamido linker are new.

DETAILED DESCRIPTION - Fluorescent cyanine compounds of formula (I) containing a sulfonamido linker are new:

X1, X2 = -0-, -S-, -CMe2 or -C=CH2;

- Y1, Y2 = non-metal atoms required to form a benzo-condensed or naphtho-condensed ring;
- Q = a conjugated moiety that increased the fluorescent
 quantum yield and stability of (I);
- R1, R2 = H, 1-4C alkyl, 1-4C alkylensulfonic or 1-4C alkylensulfonate group;
- R3, R4, R5 = H, sulfonic, 1-4C alkylensulfonic, 1-4C alkylensulfonate or SO2NH(CH2)m-W-(CH2)nZ;
 - W = absent or -SO2NH-, -O-, -COO or -CONH-;
- n, m = 0-12; provided that m+n = at most 12 and at least 1 of m and n is 0;
- Z is or contains a N, O, S nucleophilic functionality, or a functionality capable of reacting with N, O or S nucleophiles;
- provided that at least 1 of R1-R5 contains a sulfonic or sulfonate group.

INDEPENDENT CLAIMS are included for:

ΤI

MC

TT

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(a) nucleic acid probes, immunologically binding reagents,
     nucleotides and nucleosides labelled with (I); and
          (b) (2) use of the nucleic acid probes and immunologically
     binding reagents labelled with (I) for assay of an analyte in a
          USE - (I) are useful as labels in immunoassays, for
     detection of nucleic acids (RNA and/or DNA), and for labelling
     probes for DNA sequencing.
     Dwg.0/57
     New fluorescent cyanine labels containing
     sulfonamido linker.
          1065250
                   UPAB: 20051216
     NOVELTY - Fluorescent cyanine labels containing a
     sulfonamido linker are new.
          DETAILED DESCRIPTION - Fluorescent cyanine compounds of
     formula (I) containing a sulfonamido linker are new:
          X1, X2 = -0-, -S-, -CMe2 \text{ or } -C=CH2;
          Y1, Y2 = non-metal atoms required to form a benzo-condensed or
     naphtho-condensed ring;
          Q = a conjugated moiety that increased the fluorescent
     quantum yield and stability of (I);
          R1, R2 = H, 1-4C alkyl, 1-4C alkylensulfonic or 1-4C alkylensulfonate
          . that at least 1 of R1-R5 contains a sulfonic or sulfonate group.
          INDEPENDENT CLAIMS are included for:
          (a) nucleic acid probes, immunologically binding reagents,
     nucleotides and nucleosides labelled with (I); and
          (b) (2) use of the nucleic acid probes and immunologically
     binding reagents labelled with (I) for assay of an analyte in a
     sample.
          USE - (I) are useful as labels in immunoassays, for
     detection of nucleic acids (RNA and/or DNA), and for labelling
     probes for DNA sequencing.
     Dwg.0/57
     CPI: B04-B03; B04-E01; B04-E05; B06-H; B11-C07B3;
          B11-C08E4; B11-C08E5; B12-K04F; D05-H09; D05-H11;
          D05-H12D1; D05-H18A; E06-H
     EPI: S03-E14H
     TT: NEW FLUORESCENT CYANINE LABEL CONTAIN SULPHONAMIDO
         LINK.
L14 ANSWER 4 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-349553 [30] WPIX
DOC. NO. NON-CPI:
                     N2000-261898
DOC. NO. CPI:
                     C2000-106227
TITLE:
                     Staining immobilized nucleic acids for detecting nucleic
                     acids in a sample by hybridizing target DNA material to
                     the DNA probes present at its proximity on a
                     solid substrate and binding a dye for
                     detection.
DERWENT CLASS:
                     B04 D16 J04 S03
INVENTOR(S):
                     FOOTE, R S; JACOBSON, S C; RAMSEY, J M
PATENT ASSIGNEE(S):
                     (LOCK) LOCKHEED MARTIN ENERGY RES CORP
COUNTRY COUNT:
PATENT INFORMATION:
    PATENT NO
                KIND DATE WEEK LA PG
    US 6056859 A 20000502 (200030)* 12
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APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6056859	A	US 1997-800241	19970212

PRIORITY APPLN. INFO: US 1997-800241

19970212

AN 2000-349553 [30] WPIX

AB US 6056859 A UPAB: 20000624

NOVELTY - Staining immobilized nucleic acids by affixing a DNA probe to a solid substrate (12), with a disposed channel, of a microchip structure (10), hybridizing to the target DNA molecule which is passed through the channel and binding a fluorescent dye, which is moved through the channel under the influence of an externally applied electric potential, to the hybridized complex for detection, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the apparatus useful for staining and detecting immobilized nucleic acids, comprising a solid substrate, with at least one disposed channel, affixed to a DNA probe, a device for moving target DNA material through the channel into the proximity of the DNA probe for hybridization, a device comprising an externally applied electric potential for moving a fluorescent dye into the proximity of hybridized complex for its binding and a detector for detecting the fluorescence of the hybridized, dye bound DNA at the hybridization site of the channel.

USE - For staining and detecting immobilized nucleic acid molecules (claimed) in biological samples for clinical and biological experiments.

ADVANTAGE - Pre-labeling in hybridization arrays is avoided as the technique is simple and has potentially improved detectability.

DESCRIPTION OF DRAWING(S) - The figure shows the microchip structure useful for staining immobilized nucleic acids.

Microchip structure 10 Solid substrate 12

Dwg.1/6

- TI Staining immobilized nucleic acids for detecting nucleic acids in a sample by hybridizing target DNA material to the DNA **probes** present at its proximity on a solid substrate and binding a **dye** for detection.
- AB US 6056859 UPAB: 20000624 NOVELTY - Staining immobilized nucleic acids by affixing a DNA probe to a solid substrate (12), with a disposed channel, of a microchip structure (10), hybridizing to the target DNA molecule which is passed through the channel and binding a fluorescent dye , which is moved through the channel under the influence of an externally applied electric potential, to the hybridized complex for. . . staining and detecting immobilized nucleic acids, comprising a solid substrate, with at least one disposed channel, affixed to a DNA probe, a device for moving target DNA material through the channel into the proximity of the DNA probe for hybridization, a device comprising an externally applied electric potential for moving a fluorescent dye into the proximity of hybridized complex for its binding and a detector for detecting the fluorescence of the hybridized, dye bound DNA at the hybridization site of the channel.

USE - For staining and detecting immobilized nucleic acid molecules (claimed) in biological samples for clinical and biological experiments.

ADVANTAGE - Pre-labeling in hybridization arrays is avoided as the technique is simple and has potentially improved detectability. DESCRIPTION OF DRAWING(S) -. TECH UPTX: 20000624 TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Preferably, both DNA probe and the target molecule are simultaneously moved to the solid substrate for hybridization. At least one DNA probe is affixed substantially throughout the length of at least one channel of the substrate, and target DNA, fluorescent dye and other reagent are transported through the channel. Target DNA and fluorescent dye are moved by applying electric potentials across the channel so as the impart electroosmotic or electrophoretic movement of the target DNA to the probe. Fluorescent dye is further moved by applying hydraulic pressure to the channel. Multiple DNA probes are affixed to the discrete site within the channel of the microchip structure. Preferred Apparatus: The solid substrate has channel patterns including the number of channels for the movement of target DNA and the fluorescent dye. A device for applying the hydraulic force to at least one channel at a level sufficient for moving target DNA to the probe is also provided. Preferred Oligonucleotides: Probe and target material are preferably RNA material. Oligodeoxynucleotides, oligoribonucleotides, peptide nucleic acids and oligonucleotide analogs containing modified internucleotide linkages such as phosphotriester, phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, carbonate, carboxymethyl, acetamidate, carbamate, peptide, thioether, sulfonate, sulfonamide, sulfamate, sulfide, sulfoxide, sulfone, formacetal, thioformacetal, methylhydroxylamine, N-cyanoguanidine or alkylsilyl linkages. Oligonucleotide analogs contains a modified sugar such as 2'-halo, 2'-O-alkyl or 2'-O-allyl ribose sugars or a modified heterocyclic base comprising 5-fluorouridine,. MC CPI: B04-E01; B04-E05; B11-C07B3; B11-C08E5; B12-K04F; D05-H09; D05-H10; D05-H12A; D05-H12B; D05-H12D1; D05-H12D6; D05-H13; D05-H18; J04-B01 EPI: S03-E03 TT: STAIN NUCLEIC ACID DETECT NUCLEIC ACID SAMPLE TARGET DNA MATERIAL DNA TT PROBE PRESENT PROXIMITY SOLID SUBSTRATE BIND DYE L14 ANSWER 5 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN ACCESSION NUMBER: 2000-104606 [09] WPIX CROSS REFERENCE: 2001-662458 [70] DOC. NO. CPI: C2000-031317 TITLE: Nucleic acid hybridization assay composition for hybridization assay procedures. DERWENT CLASS: B02 B04 D16 INVENTOR(S): HURLEY, I; RABBANI, E PATENT ASSIGNEE(S): (ENZO-N) ENZO DIAGNOSTICS INC COUNTRY COUNT: PATENT INFORMATION: PATENT NO KIND DATE WEEK LA PG A 19991207 (200009)* US 5998135 53 US 6239271 B1 20010529 (200132) APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5998135	A Cont of	US 1989-314995	19890224
	Cont of	US 1994-194215	19940209
		US 1995-486053	19950607
US 6239271	B1 Cont of	US 1989-314995	19890224
	Cont of	US 1994-194215	19940209
	Cont of	US 1995-486053	19950607
		US 1999-386695	19990831

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6239271	B1 Cont of	US 5998135
PRIORITY APPLN. IN	NFO: US 1989-314995 1994-194215 1995-486053 1999-386695	19890224; US 19940209; US 19950607; US 19990831
AN 2000-104606	-	19990031

CR 2001-662458 [70]

AB 5998135 A UPAB: 20011227

> NOVELTY - A nucleic acid hybridization composition (I), comprising nucleotides bound to a lanthanide metal or fluorophore (acting either as energy donor or acceptor) and a solid matrix with two intercalators attached to its surface (one intercalator is capable of capturing double stranded nucleic acid (dsDNA) and the other optionally comprises a fluorophore (both act as energy donors or acceptors)), is new.

DETAILED DESCRIPTION - A nucleic acid hybridization composition comprises oligo/polynucleotides bound (directly or indirectly) to a lanthanide metal or a fluorophore (acting either as energy donor or acceptor) and a solid matrix with two intercalators attached. One is capable of capturing a dsDNA and the other optionally comprises a fluorophore. Both of them act as either energy donors or acceptors. Upon hybridization of the oligo/polynucleotide to a complementary polynucleotide, energy is transferred from the donor to the acceptor (which are positioned within close proximity to allow this).

INDEPENDENT CLAIMS are also included for the following:

- (1) a nucleic acid hybridization assay process for detecting the presence of nucleic acid sequences of interest, comprising contacting the sample containing the nucleic acids of interest (in a single stranded form) to (I) and detecting the energy emitted from the energy acceptor;
- (2) a kit comprising (in a packaged combination) reagents for detecting the presence of nucleic acids in samples, comprising a container with solid matrices bound to its surface with a first intercalator capable of capturing dsDNA, a second container with a hybridizable oligo/ polynucleotide bound (directly or indirectly) to a lanthanide metal or fluorophore (acting either as energy donors or acceptors) and final container for a second intercalator optionally bound to a fluorophore (acting either as energy donors or acceptors) (the fluorescent emissions of the first and second intercalators have different wavelengths).

USE - In hybridization assay techniques for detecting the presence of an analyte by means of energy transfer.

ADVANTAGE - Use of intercalator bound solid matrix serves to capture and concentrate the duplexes formed between the target

polynucleotide and the probe. This allows hybridization with significantly more rapid rates. The detection complex is present on the surface, therefore it is more completely and precisely localized for generating a much stronger signal. Since the intercalator serves to capture the hybrid, background emission is reduced, subsequently resulting in more accurate quantitative determination of target polynucleotides.

Dwg.0/0

AB US 5998135 UPAB: 20011227

NOVELTY - A nucleic acid hybridization composition (I), comprising nucleotides bound to a lanthanide metal or fluorophore (acting either as energy donor or acceptor) and a solid matrix with two. . . fluorophore (both act as energy donors or acceptors)), is new.

DETAILED DESCRIPTION - A nucleic acid hybridization composition comprises oligo/polynucleotides bound (directly or indirectly) to a lanthanide metal or a fluorophore (acting either as energy donor or acceptor) and a. . . the other optionally comprises a fluorophore. Both of them act as either energy donors or acceptors. Upon hybridization of the oligo/polynucleotide to a complementary polynucleotide, energy is transferred from the donor to the

acceptor (which are positioned within close proximity to allow this).

INDEPENDENT CLAIMS. . . solid matrices bound to its surface with a first intercalator capable of capturing dsDNA, a second container with a hybridizable oligo/polynucleotide bound (directly or indirectly) to a lanthanide metal or fluorophore (acting either as energy donors or acceptors) and final container for a second intercalator optionally bound to a fluorophore (acting either as energy donors or acceptors) (the fluorescent emissions of the first and second intercalators have different wavelengths).

USE - In hybridization assay techniques for detecting the presence. transfer.

ADVANTAGE - Use of intercalator bound solid matrix serves to capture and concentrate the duplexes formed between the target **polynucleotide** and the **probe**. This allows hybridization with significantly more rapid rates. The detection complex is present on the surface, therefore it is more. . . the intercalator serves to capture the hybrid, background emission is reduced, subsequently resulting in more accurate quantitative determination of target **polynucleotides**.

Dwg.0/0

TECH

MC

UPTX: 20000218

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Arrangement: Proximate distance between the **oligonucleotides** and sample the **nucleotide** is equal to or less than Furster's radius (preferably it is 30 Angstromdegrees or less).

Preferred Metals: The lanthanide metal may. . . penta acetic acid (DTPA) or with trans diaminocyclohexane tetra acetic acid (DCTA). A lanthanide chelate may be bound to the oligo/polynucleotide by a linkage group which may be allylamine.

Preferred Compounds: The fluorophore selected may be a naphthalene sulfonamide or a pyrene compound. The first intercalator is bound to the surface by a linkage group. The solid matrix comprises. . CPI: B04-E01; B04-E05; B11-C08E5; B12-K04A;

B12-K04E; B12-K04F; D05-H02; D05-H09; D05-H10; D05-H12D1; D05-H18

L14 ANSWER 6 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN ACCESSION NUMBER: 2000-013268 [01] WPIX DOC. NO. NON-CPI: N2000-010275

sample (S1), while another enzyme (E2) is used as a label for the bound target sample (S2). Sample (S1) is reacted with chemiluminescent peroxidase-substrate and a peroxide to produce the chemiluminescent signal. This signal of sample (S1) is detected. Sample (S2) is reacted with chemiluminescent substrate, specific to its labeled enzyme and an inhibitor of peroxidase enzyme, which terminates the chemiluminescent signal of sample (S1) and produces the chemiluminescent signal of sample (S2), which is then detected.

USE - The method is useful for determining presence of genetic mutations (claimed), for multiplex DNA sequencing (claimed), for DNA finger printing, for detecting several DNA markers or probes on a single Southern blot.

ADVANTAGE - The sequential detection method eliminates the need to strip and reprobe Southern, Northern and Western blots. Dwg.0/4

TΙ Method of sequential chemiluminescent detection of two uniquely labeled DNA samples, used for determining presence of genetic mutations and DNA sequencing. AΒ

- Two target samples (S1,S2) are immobilized and bonded with specific binding agents (B1,B2) to form a pair of uniquely labeled target samples. The sample S1 is detected using peroxidase enzyme substrate complex, while the sample S2 is detected by a. . . contacted with respective binding agents (B1,B2) to form two bonded pairs of target samples. Peroxidase enzyme is used as a label for the bound sample (S1), while another enzyme (E2) is used as a label for the bound target sample (S2). Sample (S1) is reacted with chemiluminescent peroxidase-substrate and a peroxide to produce the chemiluminescent signal. This signal of sample (S1) is detected. Sample (S2) is reacted with chemiluminescent substrate, specific to its labeled enzyme and an inhibitor of peroxidase enzyme, which terminates the chemiluminescent signal of sample (S1) and produces the chemiluminescent signal. . . presence of genetic mutations (claimed), for multiplex DNA sequencing (claimed), for DNA finger printing, for detecting several DNA markers or probes on a single Southern blot.

ADVANTAGE - The sequential detection method eliminates the need to strip and reprobe Southern, Northern and Western blots. Dwg.0/4

TECH

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UPTX: 20000105 TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: B1 is labeled with a hapten (H1) and B2 is labeled with H2, which is different from H1. The peroxidase enzyme is conjugated with a binding agent B3 which binds to H1 and E2 is conjugated with a binding agent B4 which binds to H2. Alternately, B1 is directly labeled with peroxidase enzyme and B2 is directly labeled with E2. Samples S1 and S2 are proteins which are detected by Western blot assay method. Preferred Compounds: The haptens H1 and H2 are chosen from biotin, fluorescein and digoxigenin. The chemiluminescent substrate for E2 is an enzymatically triggerable dioxetane of formula (I) and (II): A1 and A2 = \cdot . general formula (III): R = alkyl, heteroalkyl, aralkyl groups; R1-R8 = light producing groups; C(=0)-Y= ester, thioester or sulfonamide.

A groups adjacent to R1-R8 can constitute the group CH=CH-CH=CH, hence forming benzo fuzed ring. Alternately, the N-alkylacridan-9-carboxylate derivative has formula. . . binding agents B1 and B2 (which have the respective complementary nucleic acid sequences) get bonded. The sample S1 contains the nucleotide sequence of a normal gene and sample S2

contains the sequence of a mutated gene.
Preferred Materials: The solid support. . .

MC CPI: B01-D01; B04-B03C; B04-B04C7; B04-E01; B04-E02B; B04-E03B;
B04-E05; B04-G01; B04-L01; B04-L03B; B05-B01N; B05-C07;
B05-C08; B06-A02; B06-D11; B06-F03; B07-A04; B07-D09; B10-A15;
B10-A16; B11-C07A4; B11-C07B4; B11-C08D1; B11-C08E3; B11-C08E4;
B11-C08E5; B12-K04F; B12-M09; B14-D05B; D05-A01A;
D05-A01B1; D05-H09; D05-H10; D05-H12B1; D05-H18A
EPI: S03-E04E; S03-E14H; S03-E14H4